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THE CARDIOVASCULAR EXAMINATION OF THE ARMY RECRUIT*

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IT is obvious to anyone who has followed the course of the present war that a high degree of stamina is vital to the modern soldier, perhaps even more so than ever before. It is necessary, therefore, to adhere to the strictest standards when deciding whether or not a man should be classified as "fit for general military service." In reaching a conclusion, one must visualize as nearly as one may from this present distance the rigors of modern warfare, and furthermore, the examiner must bear in mind the question of possible future compensation arising from a certificate of disability discharge.

Criteria that might rightly be applied to civilian life may not be proper for the modern military regime, and it should be constantly remembered that the army of today functions more than ever as a unit and that even the temporary disability of one man may be of grave import to the unit as a whole. Moreover, it is probably incorrect to assume that because a man has been "athletic" in civil life he will necessarily be able to endure the hardships of an extended and concentrated campaign under modern conditions. One professional athlete who had successfully participated in his chosen vocation in October, 1940, was properly rejected by the United States Army for gross physical defects a month later. In this respect, Paragraph 1-*b* in A. R. (Army Regulations) 40–105 is worth recalling: candidates for commissions in the organized reserves "must be free from any defect or pathological condition which would interfere with the performance of the duty expected of them in the Army, or which would, as a result of service, be especially liable to undergo progressive change or to become the basis for a claim against the Government in the event of call to active service."

This communication is concerned only with the cardiovascular system of the recruit, and much has been learned in this respect in the past twenty-five years. The standards relative to other body systems should be quite as exacting.

Up to May, 1918, "heart disease" ranked third in the list of causes of discharge from the British Army and the Royal Navy,[1] yet in 1938, diseases of the circulatory system accounted for but one tenth of the annual death rate in the United States Army.[1] It is problematical whether this major difference is due to increased attention to the cardiovascular system, to the reduction of the incidence in certain diseases leading to cardiovascular disorders or to the fact that from 1914 to 1918 the British forces were actually at war. It is likely that all these factors are involved. On the other hand, it is interesting that only 0.8 per cent of 37,000 men at Camp Devens up to May, 1918, were rejected for cardiovascular disorders,[2] and that during World War I approximately 0.5 per cent of all men drafted and sent to military camps were rejected for cardiovascular defects.[3] It should be especially noted that neither of these statistical analyses includes those men rejected by their local draft boards. The figures cited correspond more closely to those of the present induction centers (now designated as examining centers). The Metropolitan Life Insurance Company rejects as "ineligible for standard life insurance" approximately 2 per cent of all applicants below the age of thirty-five. Preliminary figures show that, in the past year, slightly over 3 per cent of all men have been rejected for cardiovascular disease by their local examining boards.[4, 5]

The various induction centers of the United States Army are guided in their selection of men by regulations covered in M. R. (Mobilization Regulations) 1-9. At these centers, only men are examined who have been passed as physically fit for general military service by their local selec-

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tive-service boards, together with those men applying for regular enlistment in the Army and a certain number of aviation cadets who have been, or will be, examined further by a flight surgeon.

Under Paragraph 55 of M. R. 1-9, it is apparent that to be placed without question in Class 1-*A* (general and unlimited military service) a man must have a cardiovascular apparatus free of all but the most trivial deviations from the strict normal. The apex impulse must be within the midclavicular line, and no thrills or "important murmurs" may be present. The pulse rate must be under 100 and over 50. No cardiac arrhythmias are allowed other than sinus inequality and infrequent extrasystoles. More than transitory hypertension patently due to excitement is disqualifying. Neurocirculatory asthenia, unless mild, is likewise a cause for rejection. All this is as it should be, and it must be especially noted that, at present, the induction centers — in contrast to the local examining boards — either flatly accept or reject a man. The Army does not now consider Class 1-*B* (limited service), except under very special circumstances requiring a waiver from the War Department. In this respect, the induction centers differ from the local examining and advisory boards, which may, at their discretion, place a man in Class 1-*A*, 1-*B* or 4.

However, according to the same regulations, it is incumbent on examining physicians to accept for service men with "accidental functional murmurs" or with other findings that do not indicate disease or impair the selectee's ability to undergo severe bodily exertion, and to exclude those with defects, however innocent, appearing at the time of examination that would interfere with their activities (Paragraph 60, M. R. 1-9).

As a result of the experience of eleven months at the Boston Induction Center, Fourth Recruiting Area, and with the help of several cardiovascular experts, certain conclusions — subject to subsequent change — have been drawn. It seems worth while to bring these conclusions to general attention for future reference and, perhaps, amendment.

* * *

It is obvious that all recruits with organic heart disease of whatever nature should be summarily rejected (Paragraph 57, M. R. 1-9).

No recruit should be accepted if he has a diastolic murmur at either the apex or the base.

It is probably best that all recruits having an undoubted history of rheumatic fever should be rejected, even if there is no demonstrable cardiac damage at the time of examination. The possibility of recurrent rheumatic disease and of late development of valvular or myocardial disease must be considered. It is obvious that certain men may wittingly and with malice aforethought feign such a history. In such cases, documentary evidence from the patient's physician or hospital records is of the greatest value. On the other hand, men may knowingly conceal their past disease, although there are severe penalties for so doing. In such cases, a history of repeated nosebleeds, continued unexplained fever or chorea (infrequently associated by recruits with rheumatic fever) may be of some help. Recently, a man was accepted by the internist only to be rejected by the neurologist, who elicited an unquestionable past history of chorea of many weeks' duration. In doubtful cases, an electrocardiogram and six-foot film of the heart should be taken before final acceptance or rejection.

All applicants showing arteriosclerosis or arteriolar sclerosis should be rejected.

Any gross inequality of the pulse should be a cause of rejection. It is commonly taught that excitement, sleeplessness, alcoholic excesses and the like predispose to extrasytoles, yet I have been surprised to find how rare this irregularity is in recruits or selectees, even though many of them have been subjected to one or all of the supposed inciting causes. This paradoxical experience should serve to emphasize the importance of any notable arrhythmia.

The question of the significance of systolic murmurs is as difficult at induction centers as in civil life. It seems reasonable that the presence of a low-pitched, soft, systolic murmur localized at the pulmonary-valve area, or even heard at the apex, unaccompanied by other cardiac abnormalities and not preceded by a history of rheumatic fever or chorea, may be regarded as of no consequence, especially if the man appears otherwise healthy and robust. A mitral systolic murmur accompanied by an increased pulmonic second sound, slight cardiac enlargement and a history of rheumatic fever is, on the other hand, obviously a cause for rejection. Between these two extremes lie many cases. There are competent cardiologists who believe that a systolic murmur at the apex, even though loud and transmitted to the axilla, if unaccompanied by other signs should be regarded as consistent with good health. This may well be true in civil life; it is probably not true in war, and there is some evidence that even in civil life such a murmur cannot be dismissed too lightly.[6, 7] In this respect, the opinions of Bourne[8] are of interest. Discussing the examinations of the heart in British recruits, this author says: "If a systolic murmur is entirely absent in the erect position, it is unlikely to be organic. If

present only in the erect position, it is almost certainly functional in type. If absent during phases of respiration, it is unlikely to be organic." Essentially the same views are expressed by Parkinson.[9] It is undoubtedly wise to reject any man who shows a loud, harsh, systolic murmur transmitted to the axilla *even though such a murmur is unaccompanied by other pathologic signs.* That this dictum is contrary to the teachings of some is fully recognized. The opinion has not been hastily formed.

Mitral "presystolic" murmurs are also difficult to appraise. The truly presystolic murmur — especially if of the rough, crescendo type, accompanied by a loud snapping first sound and increased by exercise — should be regarded as a cause for rejection. In many cases, however, a selectee or recruit may come to the induction center with a pronounced tachycardia, and in these men one not infrequently hears what seems to be a presystolic murmur. It is in actuality more a grating quality to the first sound in an overactive heart, and it almost always disappears if the man lies down for half an hour. Such a murmur may be disregarded if no other abnormalities are present and if the past history is negative.

Men with pulse rates of 100 or over should be rejected unless the tachycardia subsides with adequate rest. It is essential to distinguish between the tachycardia caused by an unstable and nervous temperament and that patently due to excitement, temporary nervousness or lack of sleep. The latter type will almost invariably subside after half an hour's or an hour's recumbency with the added distraction of watching others undergo their examinations. It is obvious that acute infections may similarly be accompanied by tachycardia; usually, the site and nature of the infection can easily be found. Tachycardia that does not subside during the day of examination should probably be regarded as evidence of an unstable cardiovascular or nervous system and should therefore be considered a cause for rejection: a man on active service can scarcely demand a "few days' rest." If the tachycardia is the only abnormality, the examiner may be justified, in rare cases, in asking the man to return on another day for a second examination. Initial rates of 130 or over very seldom come down to normal. Marked tachycardia may follow the use of certain drugs either for therapeutic purposes or because the man being examined is a malingerer. This possibility should always be borne in mind, although not many such cases have been recognized at the Boston Induction Center.

The question of blood pressure is a most difficult one. The regulations (M. R. 1-9) state that men should be rejected who have a "persistent blood pressure at rest above 150 millimeters systolic or above 90 diastolic, unless in the opinion of the medical examiner the increased blood pressure is due to psychic reaction and not secondary to renal or other systemic disease." When the first inductions took place in Boston in November, 1940, it was the opinion of one cardiovascular expert that, for all practical purposes, blood-pressure readings could be dispensed with, since the number of true hypertensive patients in this age group would be negligible. This view has gradually been modified, and blood pressures are now taken on all men with initial pulse rates of over 100, on all men showing more than a slightest possible trace of albumin and on all obese applicants. If the blood pressure is more than 150 systolic or 90 diastolic, the recruit is rested until either the pressures have become normal or it is apparent that they will remain elevated during the day of examination. The original practice of having men return on subsequent days for further check-ups has been discarded. If rest for three days is needed to attain normal readings, it is probable that the applicant has either essential high blood pressure or neurocirculatory asthenia. In this area, we have not, so far as we are aware, encountered blood pressures elevated because of drug addiction. In other parts of the country, such falsely elevated blood pressures are not uncommon. The possibility of malingering should always be borne in mind. Adopting a long range and conservative view, and influenced by the work of Hines,[10] we now reject men whose systolic blood pressures remain over 150 and whose diastolic pressures remain over 90 during the day of examination. Grossly elevated blood pressures frequently fall to strictly normal limits within an hour. Such variations from the normal may probably be disregarded.

Neurocirculatory asthenia is, according to Bourne,[8] the "commonest cause of cardiovascular breakdown under the strain of active service." The subjects are usually high strung, repressed, fastidious in their habits and subject to palpitation, precordial distress, abnormal sweating and dyspnea or dizziness on exertion. Occasionally, the dyspnea may be extreme. There is usually an associated tachycardia. The blood pressure, particularly the systolic, tends to be elevated but variable. Sighing and yawning are common stigmas. This condition, which is probably of nervous rather than of cardiac origin, calls for sum-

mary rejection unless it is very mild. It should be noted that the syndrome is rather closely simulated in men who have, the night before examination, been on an alcoholic debauch.

* * *

When all is said and done, it must be admitted that a man is no stronger than his cardiovascular system, and that this system may be subjected to very severe strain over an indefinitely long period. We are increasingly convinced that the cardiovascular standards for admission to the United States Army should be of the strictest sort.

Tables 1 and 2, which are derived from the work sheets of the Boston Induction Center, Fourth Recruiting Area, reflect this increasing conservatism and indicate in a general way the causes of rejection for cardiovascular defects.

TABLE 1. *Rejections Due to Cardiovascular Abnormalities in 1940 (8708 Men).*

CAUSE OF REJECTION		NO. REJECTED
Essential hypertension		39
Rheumatic heart disease		15
Mitral stenosis	4	
Aortic regurgitation	2	
Mitral regurgitation	1	
Unspecified	8	
Neurocirculatory asthenia		6
Organic heart disease, type unspecified		4
Tachycardia		4
Hypertensive heart disease		1
Auricular fibrillation		1
Total rejections for cardiovascular disease		70
Percentage of total examinations		0.8
Percentage of total rejections		4.9

It should be noted that the number and percentage of rejections for cardiovascular disease during the second period were materially greater than those during the first. This difference is due to the increasing belief on the part of the examiners that the standards for acceptance (Class 1-*A*) must be of the strictest sort. This opinion has been concurred in by recognized cardiovascular experts.

TABLE 2. *Rejections Due to Cardiovascular Abnormalities in 1941 (8627 Men).*

CAUSE OF REJECTION		NO. REJECTED
Essential hypertension		88
Rheumatic heart disease		39
Mitral disease	14	
Aortic disease	2	
Mitral and aortic disease	1	
Unspecified	22	
Neurocirculatory asthenia		36
Organic heart disease, type unspecified		10
Tachycardia		8
Congenital heart disease		2
Auricular fibrillation		1
Paroxysmal tachycardia		1
Multiple extrasystoles		1
Total rejections for cardiovascular disease		186
Percentage of total examinations		2.1
Percentage of total rejections		13.3

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NEW PHYSICAL STANDARDS FOR ARMY PILOTS

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CIVILIAN physicians are aiding the national wartime program greatly through their work in examining selective-service registrants both as voluntary examiners for local selective-service boards and as specialists at Army induction centers. As a result, many physicians are informed about the physical standards required for general military service. There is a different and higher standard, however, for military aviation. With this phase of physical examination for military service, private physicians have had little opportunity to become familiar. This paper describes briefly the requirements for qualification as an airplane pilot in the Army of the United States, as changed December 17, 1941, to meet wartime requirements.

Why should a private physician know something of this? In the first place, there is the medical man's catholic interest in affairs pertaining to his profession. Beyond that, the medical profession has already indicated its zeal in furnishing all possible assistance to the Nation during the present emergency. Such information as this article provides should fit a physician more fully for possible future service of even wider scope.

For those in private practice, there is also a service to be rendered to their patients in this connection. During the month of July, 1941, nearly 1300 New England men between the ages of twenty and twenty-six years, inclusive, applied for examination as Army aviation cadets. Before making official application, many of them went to their own physicians for advice about whether their physical condition warranted the effort and expense of securing an examination from the United States Army. Seldom was the physician in a position to offer advice based on a knowledge of the requirements.

No private doctor is authorized to qualify physically a candidate for the Army Air Corps. Official qualification must be determined by a special Army examining board, which includes a flight surgeon or medical officer and at least another officer. To become a flight surgeon, a medical officer must first take a special course in aviation medicine, during which he observes the effects of flight and high altitudes on physique, as well as on other phases of medicine peculiar to aviation. After successfully completing such a course, he is authorized to term himself "A.M.E." (aviation medical examiner). If he fulfills his duties in a satisfactory manner as an aviation medical examiner for at least a year, the chief of Army Air Corps may certify him as a flight surgeon.

Even though the private physician cannot qualify a candidate officially, he may be in a position to save his patient from considerable effort and disappointment—that is, he can advise certain patients who may come to him for advice about the possibility of their entering the Air Corps that they definitely will not be able to meet the physical standards. In other cases, the private physician is in a position to encourage ambitious young men to go ahead with their applications as good risks to pass the physical examination. All this would be a service to the Army as well as to the applicant. It would relieve the pressure on the Air Corps examining boards by saving them the fruitless task of examining a large number of applicants who could have been advised earlier that they were not physically suitable.

Of the 1287 men examined during the month of July, 567 were definitely rejected; 589 qualified, and 131 others were tentatively rejected, pending correction of minor defects. Since it takes an average of four hours for the complete examination of one man, the pressure on the Air Corps examining boards is obvious.

Army aviation cadets receive commissions on graduation from the course in flying; their value as future officers must be therefore considered. A number of young men who can qualify physically are not acceptable as aviation cadets because they lack qualities considered vital for a competent officer. Many of these, however, may be eligible for training as sergeant pilots.

Applicants who have had at least two years of college training are exempt from educational examination. Among such college men, the percentage of disqualification has been much smaller than among applicants who lack such training. But young men who have not had college opportunities are also eligible for aviation-cadet training if they pass a written examination in such subjects as algebra, plane geometry, plane trigonometry and English composition. Throughout New England, under the general leadership of the New England Aviation Cadet Committee, these men are being helped to prepare for such examina-

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tions by "refresher courses" given at extremely small fees through state and local departments of education, and through such fraternal and patriotic organizations as the Elks, American Legion and Veterans of Foreign Wars. It is expected that the educational requirements will be revised in the near future to meet the wartime need for manpower.

Candidates for appointment as Army aviation cadets must be male citizens (for at least ten years) of the United States, who at the time of application have reached their twentieth, but who have not reached their twenty-seventh birthday. They may be married only if they sign a statement that their dependents have other means of support. They must be of excellent character and sound physique, and in excellent health. Those who qualify have a splendid opportunity, both in the military service and for later civilian careers in private aviation. As aviation cadets, they are given thirty-five weeks of pilot training, West Point style. During this training, they receive $75 a month in addition to their food, clothing, lodging, medical and dental care, and a $10,000 life-insurance policy. On completion of the training, they are appointed second lieutenants, Air Corps Reserve, and are assigned to active duty. While on active duty, they receive an initial lump sum of $150 to cover expenses for officer's uniform, are paid $245.50 a month, and receive a cash bonus of $500 for each year they serve on active duty. Obviously, it is a most desirable appointment.

The following discussion of physical standards is based on Army Regulations 40-105, covering the physical standards and examination procedure for the Form-63 examination of candidates for commissions. These standards are modified for flying duty, particularly those of vision. Their strict observance is considered necessary for the protection of the individual concerned and of those with whom he is associated in Army Aviation.

* * *

History. An intensive examination of the past history of the candidate and of his family is conducted to determine abnormalities that might reveal disqualifying facts. In particular, the patient is questioned to determine the presence of constitutional disease, psychopathic tendencies or previous severe injuries, and evaluation is made regarding possible present or future handicaps as a result of them.

Eye examination. This is a most intensive phase of the examination, and more candidates fail to meet the eye standards than any other. Better vision is obviously necessary for an airplane pilot than for an officer in another branch of the service. The following conditions are disqualifying:

Visual acuity less than 20/20, as tested by the ordinary Snellen chart or self-illuminating test cabinet. The applicant must be able to read the "20 line" of the Snellen chart from 20 feet perfectly, and without difficulty. Candidates with superior acuity are able to read the smallest or "15 line" from 20 feet, and are given a rating of 20/15.

Trachoma, or xerophthalmia; chronic conjunctivitis; pterygium encroaching on the cornea; complete or extensive destruction of the eyelids, disfiguring cicatrices and adhesions of the lids to each other or to the eyeball; inversion or eversion of the eyelids, or lagophthalmos; trichiasis, ptosis, blepharospasm or chronic blepharitis; epiphoria, chronic dacryocystitis or lachrymal fistula; chronic keratitis, ulcers of the cornea, staphyloma or corneal opacities encroaching on the pupillary area and reducing the acuity of vision below the standard noted above; irregularities in the form of the iris, or anterior or posterior synechias sufficient to reduce the visual acuity below the standard; opacities of the lens or its capsule sufficient to reduce the acuity of vision below the standard, or progressive cataract of any degree; extensive coloboma of the choroid or iris, absence of pigment, glaucoma, iritis, or extensive or progressive choroiditis; retinitis, detachment of the retina, neuroretinitis, optic neuritis or atrophy of the optic nerve; loss or disorganization of either eye, or pronounced exophthalmos; pronounced nystagmus, or permanent or well-marked strabismus; diplopia or night blindness; abnormal conditions of the eyes due to diseases of the brain; malignant tumors of the lids or eyeballs; asthenopia accompanying any ocular defect.

Color blindness. Defects of color vision are frequently discovered in men unaware of their presence. Ishihara's or Stilling's test charts are used for the determination of color vision, in addition to the Holmgren wool yarns. Some persons can select the six cardinal colors correctly but have difficulty with the various shades or mixtures. Such men will show color defects when tested with a set of pseudoisochromatic plates (American Optical Company) or the Ishihara plates, and they are disqualified if they miss more than 25 per cent of the plates. A pilot must have normal color vision for many reasons, among others the frequent use of colored lights for night landings and signal operations. There

exists a widespread false belief that color-blind persons are accepted by the Air Corps as observers. This is a myth. The false belief has been traced to a journalist's speculation concerning whether a color-blind observer might not be effective in detecting camouflaged objects because the camouflage was designed for normal eyesight. It is an interesting speculation, but tests have not proved its truth. The value of color-blind observers in the field of camouflage detection is questionable, and candidates showing color vision defects are not acceptable for pilot training.

Ear, nose and throat. Hearing, which is tested by the whispered voice test and the audiometer, when available, must be 20/20 in each ear. On otoscopic examination, there must be no evidence of a serious past inflammatory process that has resulted in sequelas interfering with the auditory or vestibular functions. In the examination of the nose and throat, distinction is made between permanent and temporary disqualifying conditions. For example, marked chronic enlargement of the tonsils or a deviation of the nasal septum sufficient to produce mouth breathing is temporarily disqualifying. After the correction of such temporary defects, a candidate is acceptable, but any irremediable defect or abnormality that materially interferes with the respiratory or olfactory function or with phonation disqualifies permanently. Consideration will show how essential it is for a pilot to have ears, nose and throat in excellent condition, especially when he flies at high altitudes and is thus subject to conditions outside those met in earth-bound pursuits.

Dental examination. Applicants must have a minimum of twelve teeth, which must include three serviceable natural masticating teeth above and three below opposing, and three serviceable natural incisors above and three below opposing. A satisfactory fixed prosthetic appliance may be considered serviceable, provided there is no evidence of infection or degeneration resulting from the pressure caused by the appliance. On the other hand, a removable plate or bridgework is not acceptable as a replacement for natural teeth. Disqualifying dental defects include gross prognathism, gross malocclusion and chronic gum infections, such as marked pyorrhea alveolaris.

General physical examination. This is similar to the examination prescribed for selective-service trainees in Mobilization Regulations 1-9. Care is exercised to detect any abnormalities of the cardiovascular, respiratory, gastrointestinal, endocrine and genitourinary systems. Muscles, bones and joints are carefully examined to determine freedom of motion, muscular co-ordination and evidence of previous disease or injury. The existence of any form of organic heart disease is disqualifying. A systolic murmur at the apex that is transmitted to the axilla or angle of the scapula disqualifies. A cardiac murmur must be carefully investigated, and electrocardiograms and 6-foot films of the heart taken in an effort to determine whether the murmur is organic or physiologic in origin. Disqualifying is a heart rate of 100 or over, or of 50 or under, when this is proved to be persistent in the recumbent position; or a persistent systolic blood pressure of 140 or over for applicants under twenty-five years of age or of 150 or over for those twenty-five years of age or older.

Height and weight. To be eligible, a candidate must be between 64 and 78 inches in height. His weight must be between 115 and 217 pounds and must be in proportion to his height. Evidence of obesity, with retarded development of the secondary sex characteristics, or evidence of gynecomastia or cretinism is disqualifying. Cases of underweight are investigated to determine the possibility of constitutional disease, such as tuberculosis, diabetes mellitus or hyperthyroidism.

Neuropsychiatric examination. Reflexes, gait, coordination and tremors are observed for any disqualifying indications. The function of the cranial nerves is examined, and all abnormalities reported. In addition, the experienced flight surgeon estimates whether the applicant is temperamentally fitted for aviation and appears "adaptable to military aeronautics."

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It is hoped that the foregoing will give civilian physicians a better understanding of the requirements for Army aviation cadets. In addition to helping the physician advise a patient who may be considering entering the Army Air Corps, it may be a helpful guide when young men appear to request help in correcting minor defects so that they may become physically qualified. Common remediable defects include deviation of the nasal septum, hypertrophied tonsils, carious or insufficient teeth, gum infections, overweight and underweight, hernias and varicoceles.

The purpose of these regulations is to conserve life and matériel by selecting for flying duty only men who are physically and mentally fit for such duties. It is, of course, necessary to maintain this standard, and further examinations are therefore made from time to time, with the result that newly developed defects may cause reclassification into lower brackets, either temporarily or permanently.

Equipped with this information, the medical profession should be better able to help their own patients and to serve their country in promoting the slogan — "Keep 'Em Flying."

ARTERIAL OCCLUSION IN RELATION TO EFFORT*

With Special Reference to the Retinal Arteries

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AMONG the problems of industrial employment of persons with cardiovascular disease, there is none more troublesome than the determination of the relation between vascular obstruction and the work being done at the time of the attack. In coronary occlusion, evidence has failed to prove that a given physical effort can be considered responsible for the closure of the artery, although some studies suggest that subintimal hemorrhage, with or without rupture into the lumen from an atheromatous ulcer, may be precipitated by exertion. This, however, is a matter of speculation, and complete or relative inactivity appears to be the state most commonly present at the time of acute cardiac infarction.[1, 2] This observation appears statistically significant even when the usual proportionate time spent by people at rest and while exercising is evaluated.

Although cases of coronary closure during work come most frequently into court for adjudication, there are other types of arterial occlusion in which the relation to exertion becomes a matter of medicolegal interpretation, namely, peripheral embolism and thrombosis, and arterial blocking from spasm or endarteritis. Perhaps the most dramatic is that resulting in sudden loss of eyesight from obstruction to the retinal artery. A case of this sort was the stimulus to the present study.

A sixty-one-year-old man with rheumatic and arteriosclerotic heart disease and aortic stenosis was working as a janitor. He did not complain of cardiac symptoms, and the heart showed normal rhythm except for premature beats. He was tending the fires, and when he opened the furnace door, a slight explosion occurred with a puff of coal gas. He stepped back from the flash and noticed sudden loss of sight in the left eye. He continued to work and carried ash barrels in the afternoon. Following this, he noted tingling in his left arm and foot, and twelve hours later developed paralysis of this side. It was claimed that the effort and excitement of stepping back from the explosion resulted in occlusion of the retinal artery by an embolus projected from the heart. A review of our experience, which was undertaken in an attempt to discover the probabilities in such a case, was extended to involve a study of other types of arterial occlusion in ambulatory patients in relation to the precise effort that they were undergoing at the time of the attack.

It can easily be seen by a study of hospital records that most emboli, pulmonary and peripheral, occur when the patients are at rest in bed, either postoperatively or suffering from cardiac failure. We are not concerned with this group, since we are interested in discovering what a person, in a presumably ordinary condition of health, may be doing when peripheral embolism or thrombosis occurs.

The patients are divided into two groups: those with and those without eye symptoms. We have 29 patients in the former, with thirty attacks of occlusion, and 46 in the latter, with forty-seven occlusions. Both groups present diagnostic difficulties, particularly patients with retinal-artery occlusion. It is not often necessary to remove such eyes surgically, and the pathologic condition cannot be confirmed by examination. Such occlusion may be due to embolism, thrombosis, endarteritis (at times, syphilitic), prolonged spasm of the artery, as in acute quinine poisoning, aneurysm of the carotid system, cardiac inhibition from painful stimuli, severe hemorrhage, as in bleeding peptic ulcer, or combinations of these factors. In many cases, no obvious general disease is present. It should be understood that we are confining the problem to arterial and not venous occlusion. The latter is about four times as common as arterial obstruction, according to Minton.[3] The retinal picture of arterial blocking is that of ischemia, often with the characteristic cherry-red spot at the macula, and not the gross hemorrhage that is seen in venous obstruction. It seems generally agreed, however, that although embolism of the central artery of the retina remains a popular diagnosis, such embolism is relatively rare, and that obliterating endarteritis with thrombosis is the common cause. According to Kern,[4] no source of embolus can be found in over 66 per cent of the cases. However, cases of bilateral occlusion are extremely

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rare. In any event, the cardiac conditions that are most commonly associated with intracardiac thrombi should present the best presumptive background for embolism — cardiac infarction, mitral stenosis, auricular fibrillation or subacute bacterial endocarditis. This last condition does not appear in our series, since such patients are very rarely able to work beyond the earliest stages of the disease.

Several studies of the condition have been made, and many individual case reports published, particularly with reference to therapy in those with embolism, such as the use of amyl nitrite, acetylcholine, heparin and massage of the eyeball. We have failed to find any extensive series analyzed with a consideration of the exact activity at the time of the vascular accident. Minton[3] remarks that such occlusion of the retinal vessels rarely occurs in young people (10 per cent), when it is usually the result of valvular disease of the heart; in over 90 per cent of the cases, the lesion appears after fifty years of age, and is due to gradual obliteration of the arteries with final abrupt closure. In his series of 64 cases, activity of the patient at the time of the loss of eyesight is described in only 4: a twenty-three-year-old woman with mitral stenosis on getting out of bed ten days after a second delivery; a forty-seven-year-old man with a normal heart on the day following severe hematemesis; a sixty-nine-year-old man during an attack of influenza; and a forty-eight-year-old woman who was walking in the street. Minton states, however, that occlusion of the artery may occur at any time of the day, although in most cases it happens in the early hours of the morning. He believes that a slight fall in blood pressure results in a diminished flow to the retinal artery and collapse of a half-occluded vessel, with thrombosis and permanent occlusion, but admits that spasm may be a factor.

De Schweinitz and Holloway,[5] in 1908, described 5 cases: a fifty-two-year-old man with arteriosclerosis and probable hypertension, who lost his eyesight after many hours of proofreading; a thirty-two-year-old Negress with an enlarged heart and questionable syphilis, who awoke in the morning with blindness of the left eye; a thirty-two-year-old woman with mitral stenosis, who lost her vision while giving a massage treatment; a forty-five-year-old man, who became blind while reading index cards; and a nineteen-year-old boy with a normal heart, who lost his eyesight while dressing.

Coverdale,[6] in 1929, found 51 cases in the literature and added 11 of his own: a twenty-four-year-old girl with mitral stenosis, while washing her hands, became blind in the right eye; a thirty-eight-year-old woman with mitral stenosis, while riding in a bus, lost the sight of the left eye; a twenty-one-year-old woman with mitral stenosis and aortic regurgitation awoke with loss of sight in the right eye; a sixteen-year-old girl with mitral stenosis awoke with blindness of the left eye; a nineteen-year-old boy with mitral stenosis, while getting up in the morning, became blind in the right eye; a twenty-one-year-old woman with a suspicious first heart sound, while making beds, lost the vision of her left eye; a sixteen-year-old girl with a normal heart became blind in the evening, after swimming in the afternoon; a thirty-six-year-old man with mitral stenosis and aortic regurgitation, while reading after work, lost the sight of his right eye; a seventy-year-old man with an enlarged heart, an aortic systolic murmur and a complete heart block, while dressing, slipped but did not fall, and suddenly lost sight in the left eye; a fifty-two-year-old man with a normal heart, while walking, became blind in the right eye; a sixty-five-year-old man with an enlarged heart and aortic systolic murmur, while sitting down, noticed that the vision became dim in the left eye — it was better the next day, but he was almost blind the following day.

In these 20 cases from the literature, no loss of vision occurred when the patient was undergoing severe or unusual exertion; 14 cases occurred with mild or moderate effort, and 6 when the patients were at rest.

In 3 of de Schweinitz and Holloway's cases, preliminary symptoms of transient blindness or hazy vision occurred at times prior to the permanent blindness. This suggests an element of spasm or, possibly, transient ischemia from reduced blood flow and, less likely, small emboli before the complete occlusion. Both spasm and emboli small enough to pass into less important retinal vessels have been observed on ophthalmoscopic examination of the retina. Some authors have thought that spasm was precipitated by effort, and that physical exertion should be reduced in patients with a history of transient blindness. In permanent loss of vision from occlusion of retinal vessels, effort appears to play no part. The situation has been compared to angina pectoris, in which unusual effort may precipitate an attack but cardiac infarct from closure of a coronary vessel, or final cumulative ischemia, does not appear to be related to physical exertion. Similarly, it is not unusual for a patient with intermittent claudication from arteriosclerosis of leg vessels to have pain on effort, but to have the final episode, which results in gangrene, appear at rest. In such cases, com-

plete arterial occlusion may not be demonstrable in the amputated specimen.

It might be argued that an increase in the activity of the heart, resulting in increased output and blood velocity, might lead to the dislodgment of mural thrombi and thus result in embolism, and, conversely, that a slowing of the blood stream might more logically be expected to promote thrombosis in the arterial system. The findings in our cases do not support the first part of this hypothesis, if the onset of symptoms can be considered coincident with the vascular blocking.

Table 1. *Occlusion of Retinal Artery.*

Case No.	Age	Sex	Clinical Diagnosis	Cardiac Rhythm	Eye Affected	Onset of Blindness
	yr.					
1	26	M	Rheumatic heart disease; aortic regurgitation and stenosis; mitral regurgitation and stenosis.	? Auricular fibrillation	Right	On awaking in morning
2*	26	M	Rheumatic heart disease; aortic regurgitation and stenosis.	Normal	Right	While working in hospital dispensary
3	40	M	Rheumatic heart disease; aortic regurgitation and stenosis.	Normal	Right	On blowing nose while walking
4	34	M	Rheumatic heart disease; mitral regurgitation and stenosis.	Auricular fibrillation	?	While resting after long ride in automobile
5	38	M	Rheumatic heart disease	Auricular fibrillation	Left	While reading aloud
6	35	F	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
7	28	M	Rheumatic heart disease	Auricular fibrillation	Right	While stooping forward
8	29	M	Rheumatic heart disease	Auricular fibrillation	Right	While bending forward
9	20	M	Rheumatic heart disease	Normal	Right	While sitting at movies
10	22	M	Rheumatic heart disease	Normal	Right	While playing baseball
11	48	M	Rheumatic heart disease	Normal	Left	While lifting or pulling
12	48	M	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
13	46	F	Rheumatic heart disease	Auricular fibrillation	Left	While reading
14	38	M	Rheumatic heart disease	Auricular fibrillation	Right	While reading
15	49	M	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
16	55	F	Hypertension	Auricular fibrillation	Right	While dressing in morning
17	60	F	Hypertension	Normal	Left	While sweeping
18	56	F	Hypertension	Normal	Right	While doing housework
19	66	M	Hypertension	Normal	Left	While sitting at movies
20	61	M	Hypertension	Normal	Right	On bending forward while at work on automobile
21	81	F	Hypertension	Normal	Right	On awaking in morning
22	63	M	Hypertension	Normal	Right	While turning head quickly
23	61	M	Arteriosclerosis and probable rheumatic aortic stenosis	Premature beats	Left	While stepping back from furnace explosion
24	75	F	Arteriosclerosis	Normal	Left	While dressing in morning
25	44	M	Syphilis	Normal	Right	While walking about house
26	51	F	Syphilis and hypertension	Normal	Left	While ironing
27	28	M	None	Normal	Left	While walking
28	23	F	None	Normal	Right	While sleeping
29	35	M	None	Normal	Left	While listening to radio

*While lying in bed receiving digitalis, this patient had an attack of blindness in the other eye — six days after an attack of paroxysmal auricular fibrillation.

Review of Cases

Occlusion of Retinal Artery

The series of cases with occlusion of the retinal artery or its branches included 29 patients, with thirty attacks (Table 1).

Fifteen cases of rheumatic heart disease were studied. The ages ranged from twenty to forty-nine years. There were 12 men and 3 women. One man had two occlusions. Nine patients had auricular fibrillation, 5 had normal rhythm, and 1 had questionable auricular fibrillation. Loss of sight came suddenly in the right eye in 10 cases, and in the left in 4. In 1 case with aortic stenosis and regurgitation and normal rhythm (Case 2), the right retinal artery was occluded first, and then the left.

It can be said that only 2 of these patients with a total of sixteen occlusions were undergoing unusual physical effort when overtaken by blindness. Six were engaged in mild exercise. Eight occlusions occurred when the patients were at complete rest. It is of interest that the man who had sudden loss of vision in his right eye on blowing his nose while walking (Case 3) was thought

possibly to have had mild typhoid fever some time before but was able to work sacking grain nine and a half hours a day without symptoms.

There were 9 cases of hypertension and arteriosclerosis, 1 of which was complicated by aortic stenosis; only 1 patient had auricular fibrillation. The ages ranged from fifty-five to eighty-one years. Five patients were women. The right eye was involved five times, and the left eye four times. Two patients were doing housework, including sweeping, 1 stepped back from a slight furnace explosion, 1 was bending forward working on an automobile, 2 were dressing, 1 awoke with loss of vision, 1 was at the movies, and 1 noticed loss of vision with a quick turn of his head. Perhaps the man at work on the automobile (Case 20) was engaged in unusual effort. The case of the janitor (Case 23) is questionable. None of the others could reasonably blame their occupations. Endarteritis with thrombotic occlusion seems the best explanation for these cases, with the possible exception of the patient with auricular fibrillation (Case 16), in whom embolism may have occurred.

Two patients were syphilitic: one, a fifty-one-year-old woman (Case 26), also had hypertension; the other (Case 25) was a man of forty-four. Both patients had normal cardiac rhythm. The woman lost the sight of her left eye while ironing, two days after premonitory symptoms lasting ten minutes. The man walked home on a cold day, drank a small glass of whisky and, while walking about the house an hour later, became blind in the right eye. No relation to effort seems apparent in these cases, and endarteritis is the probable cause. Spasm may have been a factor in Case 26.

Three patients in whom no heart or general vascular disease was found were as follows: a twenty-eight-year-old woman who went blind in the left eye while she was walking, a thirty-five-year-old man who lost vision in the left eye while sitting listening to the radio, and a thirty-three-year-old woman who became blind in the right eye while she was asleep. Blood serologic findings were negative for syphilis in all 3 cases. Two patients in this group were at rest, and 1 was engaging in mild effort.

These 30 cases of occlusion of the central artery of the retina, or its branches, occurred in 29 patients. Three patients were engaged in rather strenuous physical effort and, 15 in mild to moderate effort, and 12 were at rest.

Nonretinal Arterial Occlusion

In a series of 46 cases, with forty-seven attacks, the occlusion was not in the vessels of the eye (Table 2).

Twenty-two patients with rheumatic heart disease — 14 women and 8 men — were included. The ages ranged from twenty-six to sixty years. Four patients had normal rhythm, and 18 had auricular fibrillation; 3 had multiple occlusions. Of the whole series, 9 patients had occlusions of the cerebral vessel, 12 had occlusions in the arteries supplying the legs, and 5 had occlusions in the arms. In this group, it is likely that the occlusions were due to emboli from auricular thrombi arising from the combination of mitral stenosis and auricular fibrillation.

In no case did the embolism occur during violent effort. In 2 cases, it happened some time after unusual effort: in one (Case 43), fifteen minutes after running for a trolley, and in the other (Case 47), after the patient had fixed a bed. In 9 cases, embolism occurred during mild effort, such as rising in the morning, driving a car and eating breakfast. In this group, 2 patients (Cases 37 and 44) were somewhat more strenuous, one playing golf, and the other working as a baker. In 11 patients, or half this group, embolism occurred while the patients were at complete rest.

Twenty-three patients with arteriosclerosis or hypertension, or both, — 15 women and 8 men, — who had sudden vascular occlusions were studied. The ages ranged from forty-five to eighty-two years. One other patient, a man of forty, without demonstrable cardiovascular disease (Case 75), was also observed. He had a sudden embolus to the left posterior tibial artery, with recovery following embolectomy. The sites of the occlusion in twenty-five occlusions in 24 patients were as follows: brain, 3; legs, 19; arms, 2; and abdomen (superior mesenteric artery), 1. Auricular fibrillation was present in 10 patients (possible paroxysmal auricular fibrillation in 2), premature beats in 2, complete heart block in 1, and normal rhythm in 11. In no case was the patient engaged in severe or unusual effort, and 12 patients were at complete rest.

Discussion

It is essential to determine the relation between arterial occlusion caused by embolism, thrombosis, endarteritis or vascular spasm, and the physical effort engaged in by the patient at the time of the episode or for an indefinite interval preceding it. This relation may determine not only the responsibility of the effort for the occlusion, but also the wisdom of insisting on inactivity for victims of cardiovascular disease.

In the series here presented, embolism appears to be the likeliest mechanism for occlusion in the 38 cases in which auricular fibrillation was pres-

TABLE 2. *Peripheral Arterial Occlusion Exclusive of Retinal Vessels.*

CASE NO.	AGE	SEX	CLINICAL DIAGNOSIS	CARDIAC RHYTHM	POSITION OF OCCLUSION	ONSET OF OCCLUSION
	yr.					
30	35	F	Rheumatic heart disease; mitral stenosis.	Normal	Cerebral artery	While lying in bed three days post partum
31	56	F	Rheumatic heart disease; aortic regurgitation and stenosis; mitral regurgitation and stenosis; and hypertension.	Auricular fibrillation	Cerebral artery	While getting out of bed
32	51	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Cerebral artery	While sitting after supper
33	45	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Cerebral artery	While lying in bed
34	39	F	Rheumatic heart disease; mitral stenosis and regurgitation; and aortic regurgitation.	Auricular fibrillation	Cerebral artery	While eating breakfast
35	41	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Left leg	While lying in bed
36	59	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Left leg	While driving automobile
37	48	M	Rheumatic heart disease	Auricular fibrillation	Left leg	While playing golf
38	48	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Femoral artery	While lying in bed
39	54	M	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Right and left femoral and left brachial arteries	While working as clerk
40	49	F	Rheumatic heart disease	Auricular fibrillation	Brachial artery	While sitting in chair
41	49	F	Rheumatic heart disease	Normal	Legs, arms and brain	On awaking
42	26	F	Rheumatic heart disease	Auricular fibrillation	Cerebral artery	While sitting in chair
43	33	M	Rheumatic heart disease; mitral stenosis; aortic regurgitation.	Auricular fibrillation	Leg	Fifteen minutes after running for trolley
44	32	M	Rheumatic heart disease; mitral regurgitation and stenosis.	Normal	Left brachial artery	While working as baker
45	60	M	Rheumatic heart disease; mitral regurgitation and stenosis.	Auricular fibrillation	Left posterior tibial artery	After heavy day's work
46	39	F	Rheumatic heart disease; mitral regurgitation and stenosis.	Auricular fibrillation	Left leg	On returning to bed at midnight
47	38	M	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Left arm and (15 minutes later) both femoral arteries	After fixing a bed
48	45	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Left iliac artery	In evening while quiet
49	35	F	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Right leg	While getting out of bed in morning
50	52	M	Rheumatic heart disease; mitral stenosis.	Auricular fibrillation	Cerebral artery	While getting out of automobile
51	52	M	Rheumatic heart disease; slight aortic regurgitation; mitral regurgitation; slight hypertension.	Normal	Cerebral artery	On awaking in morning
52	55	F	Hypertension; mitral stenosis; ? rheumatic heart disease.	Auricular fibrillation	Cerebral artery	While cooking
53	56	F	Arteriosclerosis	Auricular fibrillation	Cerebral artery	While sitting talking
54	55	F	Hypertension	? Paroxysmal auricular fibrillation	Cerebral artery	While walking up hill
55	56	F	Hypertension	Auricular fibrillation	Superior mesenteric artery	While cleaning house
56	70	M	Arteriosclerosis	Normal	Left leg	While lying in bed
57	82	F	Arteriosclerosis	Auricular fibrillation	Left leg	On awaking
58	67	F	Arteriosclerosis	Normal	Left leg	While reading
59	74	M	Arteriosclerosis	Normal	Right femoral artery	Following emesis
60	51	M	Arteriosclerosis and hypertension	Auricular fibrillation	Right femoral artery	While walking
61	71	F	Arteriosclerosis and hypertension	Normal	Left femoral artery	While in bed
62	58	M	Arteriosclerosis and hypertension	Normal	Iliac artery	While working as conductor
63	64	F	Arteriosclerosis and diabetes	Auricular fibrillation	Bifurcation of iliac arteries	On awaking at 1:30 in morning
64*	45	F	Arteriosclerosis	Auricular fibrillation	Leg	While doing housework
65	59	M	Arteriosclerosis	Auricular fibrillation	Leg	While at home with cold

TABLE 2 (*Concluded*).

Case No.	Age	Sex	Clinical Diagnosis	Cardiac Rhythm	Position of Occlusion	Onset of Occlusion
	yr.					
66	50	F	Arteriosclerosis	Normal	Left leg	While sitting on doorstep
67	63	M	Arteriosclerosis and hypertension	Normal	Left leg	While sitting at supper table
68	64	F	Arteriosclerosis and diabetes	Auricular fibrillation	Both popliteal arteries	On getting out of bed in morning
69†	80	F	Arteriosclerosis and hypertension	Complete heart block	Right leg	While getting out of bath tub
70	60	F	Arteriosclerosis and hypertension	Paroxysmal auricular fibrillation or premature beats	Left brachial artery	After doing housework
71	49	F	Arteriosclerosis and hypertension	Auricular fibrillation	Right common iliac artery	While sitting on edge of bed
72	67	M	Arteriosclerosis; late syphilis; acute alcoholism.	Normal	Right popliteal artery	On awaking
73	74	F	Arteriosclerosis and hypertension	Normal, with premature beats	Left arm	While sitting after working in kitchen
74	69	M	? Arteriosclerosis	Normal	Leg	While sitting in chair
75	40	M	No heart disease proved	Normal	Left posterior tibial artery	While walking

*While lying in bed, this patient later had another occlusion in the leg.
†Patient later had an occlusion of the left arm.

ent, as well as in the 37 cases of rheumatic heart disease with or without auricular fibrillation — in 10 nonretinal cases, operation or autopsy proved this to be so. Local vascular disease, with or without spasm, was the probable cause in the other cases.

Some observers have recently suggested the transfer of the blame for sudden coronary occlusion into a rather remote past, claiming that events and activities in the life of the patient, days or even weeks prior to the occlusion, could be held responsible. Such a view opens the way to tremendous legal complications. Certainly, arterial embolism cannot be included in such a hypothesis, and this study concerns only the immediate precipitating factor. The question is, Does the effort in which the patient is engaging just prior to, or during, the occurrence of embolism have anything to do with washing off intracardiac material and releasing it into the blood stream? On a priori grounds, it seems that strenuous effort might do just this.

However, in our 38 patients with auricular fibrillation, in whom speeding of the blood stream by effort might conceivably be such an excitant of embolism, the occlusion occurred only twice a few minutes after severe effort, sixteen times with mild to moderate effort, and twenty times at rest. It may be objected that cardiac patients with auricular fibrillation, or older arteriosclerotic persons, cannot engage in violent effort to prove or disprove this assumption. Our figures suggest, however, that there is no reason to suspect that the ordinary activities of the patients' lives are likely to precipitate embolism; that unusual effort is not an expected cause of arterial occlusion; and that the mechanisms of arterial blockage are as progressive when the patient is at rest as when he is active, and perhaps more so.

In this group of seventy-seven occlusions, sudden loss of eyesight, or of the use of a limb, or occlusion of cerebral or mesenteric vessels, based on embolism or other arterial blockage, occurred during ordinary daytime activities, or when the patients were at rest, in over 9 out of 10 cases.

Summary and Conclusions

Seventy-seven attacks of acute arterial occlusion in 75 ambulatory patients are described: 30 of these occurred in the retinal arteries of 29 patients, and 47 occurred in other peripheral arteries of 46 patients.

In 3 cases, the occlusion took place during rather severe effort, and in 2, a few minutes after unusual exertion; in 37, the occlusion occurred coincident with mild or very moderate effort, and in 35, when the patient was at rest in bed or sitting in a chair.

Peripheral arterial occlusion from embolism, thrombosis or endarteritis rarely occurs during unusual physical effort even in patients with cardiovascular disease of a degree compatible with quite strenuous exertion. In our series, such occlusion occurred approximately fourteen times as

commonly when the patient was at complete rest or when engaged in the ordinary exertions of his usual life.

In approximately half the entire series of arterial occlusion, — embolic and obliterative, — the patient was physically inactive. This suggests that the conditions necessary for either embolism or thrombosis are as effective with reduced as with increased blood flow, and that the occurrence of such an accident is at least fortuitous.

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TUBERCULIN TESTS IN CHILDREN

An Interpretation of a Series of Varying Intradermal Test Doses and of a Comparable Series of Patch Tests

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IT has been the usual custom to perform the intradermal or Mantoux tuberculin test in the Out-Patient Department of the Children's Hospital by injecting 0.1 cc. of old tuberculin diluted 1:1000. As a result of this dilution, an actual dose of 0.1 mg. of tuberculin comes in contact with the intracutaneous tissues. Although a weaker initial dose is occasionally used for patients suspected of strong tuberculin allergy, experience in this clinic has not led to apprehension that more than 0.1 mg. is too great an amount for routine testing. On the other hand, some doubts have arisen that it may not be strong enough to give dependable diagnostic evidence. Since patients are frequently brought to the clinic from a considerable distance and since their transportation usually involves at least one other person, it is highly desirable that repeated visits for retesting be avoided unless there is reason to believe that a negative response to the 0.1-mg. dose is unreliable.

Although most authorities advise that patients negative to 0.1 mg. be retested with 1.0 mg. (0.1 cc. of 1:100 dilution) of tuberculin, the percentage who react only to the larger dose is variably stated. Thus, Hart,[1] in the London investigation of 1929, found that 96.3 per cent of patients with known tuberculosis reacted to 0.1 mg., and that this percentage was raised to 97.3 by retesting the negative patients with 1.0 mg. In a series of controls from the general population, he found that 40.5 per cent reacted with 0.1 mg., whereas the percentage increased to 43.5 with the stronger dose. Lincoln, Raia and Gilbert[2] have recently presented evidence to show that in New York City a much larger percentage of children negative to 0.1 mg. may react to increased doses. These authors found that 17 (10.9 per cent) of 155 such children reacted to 1.0 mg. The most striking data have come from the Lymanhurst studies. Harrington, Myers and Levine[3] published in 1937 their statistics on the sensitivity to tuberculin of over 4500 children and adolescents from five to eighteen years of age. Of this number, 8.7 per cent were positive to 0.1 mg. of tuberculin, but another 9.2 per cent of the total group were positive to 1.0 mg., although they failed to react to 0.1 mg. Thus, not even half the tuberculin-sensitive patients would have been discovered had the testing not been carried beyond the usual 0.1-mg. injection. In another context, Myers[4] cautions that "the administration of a sufficient dosage of tuberculin is important as a 10 to 20 per cent error may result from using only the small dose." Unfortunately, various series of data are not presented in a manner facilitating direct comparisons, but the experience with adults at the Boston City Hospital may be mentioned. Of 100 patients reacting to 1.0 mg. of tuberculin, 81 were found to react to 0.1, 48 to 0.01, and 14 to 0.001 mg. This indicates that an error of about 20 per cent would result from depending on 0.1 mg. as the test dose.

Such statements as these raise doubt concerning the validity of a clinic procedure in which all children negative to a routine strength of tuberculin are not called back for a stronger test. Therefore, a primary reason for the present study was to determine the error, if any, that might be avoided by performing these second tests on every infant and child not reacting to 0.1 mg.

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A second problem for consideration was the degree of reaction to which positive significance could be ascribed. This became significant particularly because of frequent errors in interpretation of tests read for us by visiting nurses and, in some cases, by health officers and family physicians. The error was almost always that of interpreting the faint redness of a dubious or negative test as positive, a mistaken impression later rectified by retesting with stronger solutions but only after considerable parental confusion, if not distress, had been brought about. In an attempt to avoid such difficulties and still to spare crowding of the clinic and unnecessary transportation of children, we now ask parents of patients living at a distance to measure the diameters of redness and of swelling at the injection site and to send us these objective data on a mimeographed postal card. Proper interpretation of such objective data requires as definite standards as possible. It should be mentioned in passing that indefinite reactions are not limited to outpatients but occasionally confuse the diagnostic data of ward patients as well, and that reference to the directions for interpreting tuberculin reactions as given in *Diagnostic Standards** does not always evaluate the dubious induration or the inconstant edema.

225
41

Experimental Procedure

A quantitative testing procedure was devised to answer the two questions, What strength of tuberculin is sufficient to elicit a positive reaction? and What local manifestations constitute such a reaction? When a child in the hospital was discovered to react to the routine test with 0.1 mg. of tuberculin, and was not deemed an unfavorable subject because of fever, serious illness or other cause, he was retested on the other arm with simultaneous injections of 0.1, 0.01 and 0.001 mg. of tuberculin, respectively, or 0.1 cc. of 1:1000, 1:10,000, and 1:100,000 dilutions. The preparation used has been standard for many years in this hospital, and consists of O.T. (old tuberculin) supplied by the Saranac Laboratories and made up to the proper strength with carbolized saline solution. Fresh dilutions are made once a month and kept in refrigerators when not in use. In some patients whose original reactions to 0.1 mg. were very slight, the graded tests consisted of 1.0, 0.1 and 0.01 mg. In all cases, the sites of injection were spaced sufficiently far apart so that resultant erythemas would not coalesce, and the strongest solution was injected proximally so that lymphatic drainage could not carry more tuberculin into sites where smaller amounts had been injected. These simultaneous graded tests were read at twenty-four, forty-eight, seventy-two and ninety-six hours thereafter, by outlining the extent of erythema and of induration on tracing paper placed over the reactions. So relatively scarce have tuberculin-positive children become in our wards that it was necessary to turn to another source to augment our series of such patients. At the North Reading State Sanatorium, through the courtesy and interest of Drs. Earle Willoughby and Gerald Caron, we were enabled to test 75 children in various stages of tuberculous disease and healing. In that institution, testing is not ordinarily made with doses stronger than 0.01 mg., and there seemed little reason for changing the procedure during this series of investigations, since children positive to 0.01 mg. would, of course, have reacted to 0.1-mg. tests also, and should give questionable reactions at the sites of still weaker doses. Accordingly, most of the North Reading children were tested only with 0.01 and 0.001 mg. of tuberculin. Some received 0.0001 mg. as well, but in every case simultaneous doses of at least two strengths were applied.

The combined groups from the Children's Hospital and the North Reading State Sanatorium furnished a total of 118 tuberculin-positive children who were tested in this general manner. In addition to these, another unselected group of about twice their number who did not react to tuberculin in the standard 0.1-mg. dose in our wards were tested with graded doses in the same way. In these, the tests usually consisted of doses of 0.1, 1.0 and 10.0 mg. Thus, 336 tuberculin-positive and tuberculin-negative children were injected with at least two and usually three simultaneous test doses (Table 1). From the results, it was possible to determine the number failing to react to 0.1 mg. but positive to 1.0 or to 10.0 mg. It was also hoped — and to some extent this hope was realized — that the responses would give some clue of what might be called a positive reaction, since weak or questionable reactions should be noted in children whose definitely positive responses to stronger amounts gave proof of their tuberculin sensitivity, just as there would also be doubtful responses in others proved by stronger tests to be tuberculin negative. Thus, a study of both types of borderline reactions might lead to criteria concerning the time of appearance and fading, degree of induration and so forth, which would guide our future interpretation of isolated questionable reactions.

This study also gave an excellent opportunity to compare the sensitivity of the Vollmer tuberculin patch test with the response of children to

*In *Diagnostic Standards*, published in 1940 by the National Tuberculosis Association, edema is considered an essential of a positive reaction; edema of more than 5 and less than 10 mm. diameter is required for a + reaction.

various strengths of O.T. administered by the Mantoux technic. Accordingly, at the time graded tests were applied to one arm, the patch test* was applied on the other arm, or more commonly on the upper back. The patches were removed after forty-eight hours, and read then and at seventy-two and ninety-six hours by the same tracing-paper technic. Thus, the study was made to answer a third question, What is the relative sensitivity of the Vollmer test as compared with the Mantoux test in various dilutions?

Results

Adequate Tuberculin Dosage

The positive reactors from Table 1 have been listed in Table 2 with the percentage of children reacting to any one dose expressed in terms of their response to a dose ten times as strong. Of 118 children who reacted to 1.0 mg., 97 per cent were found to react to 0.1 mg. Thus, in the Boston vicinity and in children younger than twelve years, the 0.1-mg. dose of tuberculin should bring to light all but 3 per cent of the positive reactors. Obviously, this will not apply everywhere, and it can be stated here only with qualifications. One reason for the practical accuracy of the test is the small number of tuberculin-sensitive persons in the clinic community, since the smaller that number is, the less frequently will one encounter the occasional state of mild allergy. A comparison of the amount of tuberculosis observed among our patients with that observed at older age levels and in different places cannot be included here. It may be stated, however, that in the last statistics available from children tested in the Out-Patient Clinic (with 0.1 mg. O.T.) the findings were: 0.7 per cent positive reactions among 190 infants under three years; 1.8 per cent among 315 children from three to five years; 2.7 per cent among 325 children from six to eight years; and 7.0 per cent among 220 children from nine to eleven years.

If 70, instead of 7, per cent of our patients reacted to tuberculin, the group requiring more than 0.1 mg. would be larger but only proportionately so, and the percentage should therefore not change. An unquestionable testimony to the comparative accuracy of the 0.1-mg. dose appears when the results are contrasted with those using 0.01 mg. It will be noted from Table 2 that 84 per cent of those reacting to 0.1 reacted to 0.01 mg., whereas only about 40 per cent of the latter group were positive to 0.001 mg. Such great discrepancies appear between graded tests weaker than 0.1 mg., and so little increase in accuracy results from tests stronger than 0.1 mg. that we shall continue to consider it a satisfactory single-strength test for routine clinic purposes. It should be mentioned, however, that in individual diagnostic problems in which the degree of allergy may be masked by fever, intercurrent infections or very early or very far-advanced tuberculosis, adaptation of the dose to the patient may be necessary. The increasing

Table 1. *Reactions to Simultaneous Tests in 119 Tuberculin-Positive and 217 Tuberculin-Negative Children Grouped according to Presumable Susceptibility.*

Group	Presumable Susceptibility of Group	No. of Cases	Reaction	Amount of O. T. in Test Dose							
				10.0 mg.		1.0 mg.		0.1 mg.		0.01 mg.	0.001 mg.
A	None	208	Positive	4		3		0			
			Negative		204		205		208		
B	Slight	13	Positive			7		6		2	
			Negative				6		7		11
C	Moderate	53	Positive					50		36	20
			Negative						3	17	33
D	Marked	62	Positive							58	18
			Negative							4	44
	Totals	336		4+	204−	10+	211−	56+	218−	96+ 32−	38+ 77−

Table 2. *Accuracy of Different Test Doses, as Shown by the Positive Reactors in Table 1.*

Group	Positive Reactors	
	1.0 mg.	0.1 mg.
A	3	0
B	7	6
C	50*	50
D	58*	58*
Totals	118	114
Accuracy of 0.1 compared with 1.0 mg.		97%
	0.1 mg.	0.01 mg.
B	6	2
C	50	36
D	58*	58
Totals	114	96
Accuracy of 0.01 compared with 0.1 mg.		84%
	0.01 mg.	0.001 mg.
C	36	20
D	58	18
Totals	94	38
Accuracy of 0.001 compared with 0.01 mg.		40%

*Not tested with this dose but reacted to weaker dose.

*The test material was kindly furnished by the Lederle Laboratories, Incorporated, Pearl River, New York.

use of P.P.D. (purified protein derivative) necessitates some expression of the results mentioned above in terms of that preparation, but only a rough comparison is possible on the basis that 0.01 mg. of O.T. is about equivalent to the first-strength dose of P.P.D., and that 1.0 mg. O.T. may not elicit quite so many positive reactions as the second-strength dose.[5] We have not adopted P.P.D. as a routine tuberculin because of its expense and because the first-strength dose is too weak and the second-strength too strong for a routine single test; nevertheless, in occasional diagnostic difficulties requiring extreme accuracy of testing, the second-strength dose is a valuable check on strong doses of O.T.

225
41

True and False Positive Reactions

The 336 patients in this study were tested with a total of nearly a thousand individual Mantoux tests (Table 1). Of this total, the interpretations of a certain number were, as was anticipated, questionable, and thus would have been, as isolated tests, dubious in significance. Their characteristics are given below. Since the results from simultaneous stronger and weaker tests were available, it was hoped that some observations might be made by which these doubtful responses could be interpreted.

There were two main groups of questionable reactions: those in children whose simultaneous stronger tests proved them to be definite reactors; and those in children whose other tests, histories and physical findings gave no evidence to suggest tuberculin sensitivity. The first group might be called "weak positive reactions," and the second "false positive reactions" or "pseudoreactions."

Weak positive tests showed an erythema 1 cm. or less in diameter, with extremely indefinite induration. Such responses, although they may fall in the + group according to *Diagnostic Standards*, and thus were listed as positives in Table 1, have occasionally been misleading and are always interpreted with hesitancy. An analysis of their characteristics as shown in this study is given in Table 3. It will be noted that an almost equal number of these weak responses was called forth by 0.001 and by 0.01 mg. of tuberculin, but their behavior was somewhat different when classified according to the dosage. Weak responses to 0.001 mg. showed a tendency to increase in area or to remain of the same size between the twenty-four hour and forty-eight-hour readings. Fading during this period was less common, so that two thirds still showed an area of erythema at least 2 mm. in diameter even after seventy-two hours. On the other hand, similar weak responses to 0.01 mg. showed less tendency to increase in area or to hold their size with the passage of time, and a smaller number persisted to three days. It appears that the weaker the test dose used, the more

TABLE 3. *Number and Behavior of Weak Reactions in Children Definitely Positive to Stronger Doses.*

Dosage and Type of Reaction		No. of Tests
Weak reactions to 0.001 mg. O. T.		33
Increased or remained of same intensity from twenty-four to forty-eight hours	22	
Faded in intensity from twenty-four to forty-eight hours	11	
Some reaction still perceptible at seventy-two hours	22	
Weak reactions to 0.01 mg. O. T.		31
Increased or remained of same intensity from twenty-four to forty-eight hours	14	
Faded in intensity from twenty-four to forty-eight hours	17	
Some reaction still perceptible at seventy-two hours	17	
Weak reactions to 0.1 mg. O. T.		2

significant is a faint type of reaction, particularly if it does not diminish in intensity after the first twenty-four hours. In fact, this series of tests shows that any response of from 5 to 10 mm. in diameter at forty-eight hours might be interpreted as positive, provided it was called forth by a dose of 0.01 mg. or, better still, by one of 0.001 mg.

It is striking that with tests of 0.1 mg., although nearly three hundred were applied and a fifth were positive, only two weak reactions occurred. In one of these children, although a definite response was obtained with 1.0 mg., the 0.1-mg. test produced only 7 mm. of erythema (no induration) at forty-eight hours and complete fading by seventy-two. In the other, the 0.1-mg. reaction reached a height of 6 mm. of erythema and 2 mm. of induration at forty-eight hours, with an impalpable 3-mm. stain at seventy-two hours.

It is difficult to speak with complete certainty of *false positive reactions* or *pseudoreactions*, since by definition they must occur in tuberculin-negative children, and the presence of any sort of response to tuberculin makes one hesitate to call a person negative. However, these reactions differed sufficiently from the weak positives just described to make us believe that they had no positive significance. It will be seen in Table 4 that they were encountered most frequently with the stronger doses, only one occurring at the site of 0.1-mg. injections and none with any weaker dose. These reactions were characterized by rapid fading; thirty subsided entirely within forty-eight hours, although many were erythematous areas 3 cm. or even more in diameter at twenty-four hours, and a few were somewhat swollen though not defi-

nitely indurated. One reaction persisted until forty-eight hours, and one did not appear before the forty-eight-hour reading. Both of these subsided completely in another twenty-four hours, leaving no sign except the needle mark. Heise and Brown[6] describe reactions to glycerin broth used in preparing tuberculin; this may be the mechanism of some of these phenomena, since their occurrence increases with the amount of O.T. used.

TABLE 4. *Pseudoreactions in Tuberculin-Negative Children.*

Dosage	No. of Tests
10.0 mg. O. T.	32
1.0 mg. O. T.	15
0.1 mg. O. T.	1
0.01 mg. O. T. or less	0
Total	48

It appears that whereas doses smaller than 0.1 mg. may not bring out tuberculin sensitivity or may elicit weak and rather insignificant reactions in positive children, doses stronger than 0.1 mg. call forth an increasing number of rapidly fading pseudoreactions. These possibilities must be borne in mind in interpreting responses to very strong or very weak solutions. Although no absolute rules of interpretation can be made from these observations, they suggest that the presence of even 2 mm. of erythema and induration at seventy-two hours indicates tuberculin sensitivity, especially if the dose employed was 0.01 mg. or less. In other words, the smaller the dose, the more attention is to be paid to faint but persistent reactions; and the larger the dose, the more a dubious reaction is likely to be of no significance, particularly if it begins to fade after the first day. Practically all the unquestionably positive reactions were marked by 1 or 2 cm. of erythema and induration and reached their maximum at forty-eight hours. At that time, the erythema was at its height, and although the induration sometimes became somewhat firmer at seventy-two hours, it was rarely any more extensive in area than before. This observation bears out the figures given by Stewart[7] regarding the growth in area of tuberculin reactions. No reactions beginning to appear later than forty-eight hours were encountered in this study, although a child has been observed in this hospital whose positive response to 0.1 mg. of tuberculin did not appear until the fourth day.

The present study indicates the advantages of the 0.1-mg. test dose, but its potential disadvantages must be considered. Lincoln and Grethmann[8] have recently called attention to the distinctly undesirable activation of disease in and around existing tuberculous foci that may result from the diagnostic injection of tuberculin. They cite 7 cases in which there was reason to believe that this had occurred. In 2 of these, the dose of tuberculin injected was 0.01, in 1 it was 0.06, in 3 it was 0.1, and in 1 several doses given within twenty-four hours made a total of 0.26 mg. Thus, dangers may be associated with comparatively small, as well as large, doses. No immediate exacerbation of pulmonary or other lesions has been observed to follow tuberculin testing in past years in this clinic, although the usual dose has been 0.1 mg. Nevertheless, a regard for the possibility of such an occurrence has often led to the substitution of weaker doses when strong allergy is suspected, and in the present investigation the proper range for simultaneous tests was established only after the relative sensitivity of the patients had been indicated approximately by previous single tests. However, the patch test was applied to all patients, some of whom (as noted below) responded with marked manifestations at its site, so that many children had simultaneous reactions to that test, as well as to two and occasionally three of the intradermal inoculations. There were no evidences of unfavorable activation around tuberculous foci. Thus, although agreeing that caution is necessary in the use of tuberculin, we believe that experience allows the recommendation of 0.1 mg. of old tuberculin as a routine dose for the Mantoux test on young patients such as those in this clinic. The use of smaller amounts is suggested for patients suspected of skeletal or lymph-node tuberculosis, pleural effusion, phlyctenular keratitis and erythema nodosum, for those with a history of long exposure to the disease, and for persons above twelve years of age. In passing, it may be mentioned that the degree of tuberculin sensitivity to the graded and measured tests in this investigation showed no relation to the extent or seriousness of the tuberculous process.

The Patch Test

Vollmer and Goldberger,[9] in 1937, introduced the application to the skin of filter-paper squares soaked with pure O.T. as a test of tuberculin sensitivity. The ease of this technic, for both physician and patient, aroused immediate interest, and the relative accuracy of the method has been indicated by several published studies recently summarized by Vollmer.[10] With one outstanding exception, the agreement between the patch and the Mantoux reactions has been quite close.

In the study here reported, 336 infants and children were tested with simultaneous patch and Mantoux tests. As shown in Table 5, no patient who failed to react to the Mantoux test gave any

reaction to the patch, so that the latter test cannot be suspected of producing false positive results, nor did it bring to light positive reactors not discovered by intradermal testing. In 113 children, there were positive reactions to both tests; among this group were several cases in which the weaker intradermal doses brought forth no response. Of the 6 patients in whom the two tests disagreed, 3 reacted only to comparatively strong intradermal doses. Thus, in this study, patients responded to the patch tests in nearly the same degree as to the 0.1-mg. intradermal doses. Apparently, except in rare cases, the patch makes a suitable screening test and would be highly efficient if followed, when negative, by a strong intradermal inoculation, such as the introduction of 1.0 mg. of O.T.

As others have observed, an occasional unpleasantly large and uncomfortable reaction to the patch test was noted, and here again the manifestations at the sites of the patch and intradermal tests ran roughly parallel. Although the actual patches of filter paper impregnated with tuberculin are only 1 square cm. in area, each of these occasionally called forth an induration of 3 cm. or more in diameter, with vesiculation and, at times, shallow ulceration. Since two such squares are present on each strip of adhesive (on either side of a control square of plain filter paper), the reactions may coalesce into a large single area. Besides these situations, it was noted that the children often spoke of itching at the patch-test sites, although there was seldom any complaint from the intradermal reactions. Vollmer[10] has pointed out the possibility of avoiding severe reactions by using weaker tuberculin solutions in the manufacture of the patches or, more simply, by leaving them in contact with the skin a shorter time.*

TABLE 5. *Comparison of Patch and Intradermal Tests.*

Result of Patch Test	Result of Intradermal Test	No. of Cases
Negative	Negative (all doses)	217
Positive	Positive (any dose)	113
Negative	Positive (0.1 mg.)	3
Negative	Positive (1.0 mg.)	2
Negative	Positive (10.0 mg.)	1

*We have made a few observations using transparent "Scotch cellulose" tape instead of adhesive and suggest it as a satisfactory backing for the test patches. The immediate surroundings of the impregnated filter-paper squares can thus be kept under observation; at the earliest sign of redness seen through the transparent tape, the whole strip can be removed. This is suggested as a means of avoiding unnecessarily prolonged application of tuberculin to the skin of very sensitive subjects.

Summary and Conclusions

Simultaneous intradermal (Mantoux) tests with graded doses of O.T. (old tuberculin) were performed on 336 infants and children under thirteen years of age. The same patients were also tested by the patch method.

Test doses of less than 0.1 mg. were less than 85 per cent as accurate as those of 0.1 mg. in revealing tuberculin sensitivity. Doses of 0.1 mg. were 97 per cent as accurate as those above that amount.

Weak positive or questionable reactions in patients with actual tuberculin allergy were usually noted in weak test doses. These reactions were characterized by a tendency to persist as mild manifestations at the site of inoculation for three or four days.

False positive reactions or pseudoreactions in patients seemingly without tuberculin allergy were the results of strong doses and may have been brought about by sensitivity to the broth. These were characterized by widespread erythema at twenty-four hours but almost complete disappearance at forty-eight.

Since the minimum number of doubtful responses was obtained with 0.1 mg. of O.T., and since this dose is only slightly, if at all, more liable to induce undesirable perifocal reactions than weaker tests are, it seems to be the most suitable amount for a routine intradermal test of clinic children in the vicinity of Boston.

The tuberculin patch test was positive in 113 (97 per cent) of 116 children who reacted to 0.1 mg. or less of O.T. by the intradermal method.

No correlation between tuberculin sensitivity and degree of infection was apparent.

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MEDICAL PROGRESS

THE ENCEPHALITIDES OF VIRUS ETIOLOGY*

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THE largest epidemic of encephalitis of known etiology that has hitherto been reported occurred during the past summer and fall.[1] Approximately 3000 persons were affected in an area encompassing the north central states and Canadian provinces. This outbreak, however, did not appear without forewarning. During the last ten years, similar but less extensive outbreaks have occurred in the Midwest,[2–8] as well as in the East[9, 10] and Far West.[11–18] The most recent epidemic appears now to be merely a higher peak in a series of recurrent waves. The clinical aspects of the disease during these outbreaks have been very similar, but have also been distinctly different from those associated with the older type of encephalitis, which appeared in 1916 and has been variously termed "epidemic encephalitis," "encephalitis lethargica" and "von Economo's disease,"[19] and the etiology of which is unknown. In the recent outbreaks, three distinct etiologic agents, all viruses, have been demonstrated. Newer developments in laboratory technic have now made it possible to identify them, to trace their distribution, and to relate them to a given outbreak. These subjects will be discussed in this report, together with a brief review of the clinical manifestations of these diseases and their treatment and prevention.

ETIOLOGY, OCCURRENCE AND DISTRIBUTION

Much confusion has existed in the past, and still exists, regarding the diagnosis of encephalitis. Thus, Wilson,[20] in a chapter on epidemic encephalitis, discusses encephalitis lethargica, Japanese B encephalitis and St. Louis encephalitis, with the implication that they are but variants of the same basic disease. Literally, the word encephalitis means "inflammation of the brain." It has been used loosely to characterize a number of clinical syndromes, — in themselves not too definite, — regardless of etiology. These clinical pictures may be produced by a variety of agents: bacteria, parasites, toxins, chemicals, viruses and, presumably, others as yet unknown. Difficulty in diagnosis and classification is almost certain to exist until the etiology of the various types of encephalitis is determined, and until the clinical criteria for diagnosis are carefully re-evaluated in the light of the etiology. Similar confusion has existed with other morbid states: pneumonia, for example, may be produced by oils (lipoid pneumonia), gases, dusts, a variety of bacteria and viruses.

During the last fifteen years, the discovery of a number of viruses affecting the central nervous system has helped to clarify the problem of encephalitis, and has permitted more or less detailed, although tentative, classifications on an etiologic basis.[21–28] For practical clinical purposes, the encephalitides of man may be divided into three groups:

Group I. Bacteria, protozoa and other parasites

Group II. Viruses
- St. Louis encephalitis
- Equine encephalomyelitis (Eastern and Western types)
- Japanese B encephalitis
- Australian X disease
- "Forest-spring" encephalitis of Russia
- Lymphocytic choriomeningitis
- Louping ill
- Virus B
- Poliomyelitis
- Rabies

Group III. Etiology unknown, possibly virus
- Encephalitis lethargica (von Economo's disease)

A number of other conditions are sometimes included in classifications of encephalitis, namely, postinfection encephalitis, postvaccinal encephalitis, postrabic-treatment encephalitis, the large group of primary demyelinating diseases and a miscellaneous group of degenerative processes caused by chemicals, toxins and so forth. No useful function would be served by including these encephalopathies in the above classification, although they must be kept in mind in differential diagnosis.

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Of these three subdivisions, only those due to specific viruses (Group II) are concerned here. Since poliomyelitis and rabies constitute special and rather well-defined problems,[29, 30] they will not be considered further.

Only two types of virus encephalitis, other than poliomyelitis, have thus far occurred in significant epidemics in this country. These are St. Louis encephalitis and equine encephalomyelitis. Other forms have occurred either sporadically, such as rabies and lymphocytic choriomeningitis, or as a result of laboratory infections, such as louping ill and virus B. Japanese B encephalitis, Australian X disease and "forest-spring" encephalitis of Russia have been epidemic in their respective countries, but have not been seen and recognized in the Western Hemisphere.

St. Louis Encephalitis

In the late summer of 1932, 38 cases of an unusual type of encephalitis occurred in Paris, Illinois.[3, 4] No etiologic diagnosis was made. The following summer, however, more than 1000 cases of a similar disease occurred during August, September and October in and about St. Louis and Kansas City.[2–4] Cases of some kind of encephalitis, possibly the same disease, had existed in this area prior to the 1933 outbreak, since in the St. Louis Children's Hospital sporadic encephalitis had shown a seasonal distribution, with a peak in July and August, during the previous fourteen-year period. In any event, a virus pathogenic for monkeys and mice was isolated in 1933 from several fatal cases[31–34] and was shown by almost all investigators[32, 35–39] to be a new, different and specific agent. This was the first outbreak of acute encephalitis in this country in which a virus was definitely established as the etiologic agent.[40]

It was found that serums from patients who had recovered from the disease contained substances that would specifically neutralize or prevent the development of infection in animals otherwise susceptible to the St. Louis virus.[32] This test therefore provided a method of determining what persons had been infected with the virus, either acutely or subclinically, as well as the geographic distribution of the disease. Thus, in the St. Louis area, it was found that serums of about 90 per cent of the convalescents and about one fifth of the "normal controls" who had not been ill contained neutralizing substances, whereas such antibodies were not found in the serums of patients with typical encephalitis lethargica (von Economo's disease), poliomyelitis and postinfection encephalitis.[41–44] Furthermore, serologic evidence indicated that the virus was not confined to the St. Louis area, but had presumably caused the outbreak in Paris, Illinois, as well as sporadic cases in New York City and the central and western states. Since 1933, repeated outbreaks have occurred in the Midwest and Far West, with apparently increasing frequency and size, and widening geographic distribution.[7, 11–15, 17, 18, 44–47] A significant factor in this process may have been the migration of labor populations from the Dust Bowl to the Far West.[48] During the last three years, cases apparently due to the virus of either St. Louis encephalitis or the Western type of equine encephalomyelitis, or both, have occurred in the same outbreaks.[6, 7, 12–15, 17, 18] With the exception of the 2 patients in New York City, no proved cases of St. Louis encephalitis have been reported from the Atlantic Seaboard.

Equine Encephalomyelitis

Until 1938, equine encephalomyelitis was considered to be primarily a disease of horses. Although the infection had probably existed on this continent for a number of years, it was first identified as a distinct entity by the isolation of the virus from horses during the 1930 epizootic in the San Joaquin Valley in California.[49] During 1931, the disease was recognized in horses throughout California, in Oregon and in Nevada.[50] In 1933, another virus was isolated from horses in the eastern section of the United States.[51, 52] These two strains of virus were found to be immunologically distinct and to differ from other known viruses.[36, 53–57] They have since been known as the Western and Eastern strains of the virus of equine encephalomyelitis. By the end of 1937, the disease was reported in all sections of the United States except New England,[58–60] and a similar disease was reported from Mexico.[61] In 1938, extensive outbreaks occurred in thirty-nine of the forty-eight states, including New England,[62, 63] and a third, distinct strain of virus was identified in Venezuela.[64] Since then, the disease has occurred in horses throughout the country.[65] Curiously enough, the western and eastern varieties of the virus have shown until recently a sharp geographic delimitation in distribution, the Appalachian Mountains providing the boundary. Both types have now been isolated in Alabama, however, and the Eastern strain has been found in Texas.[66]

The history of the recognition and apparent spread of human encephalitis due to the viruses of equine encephalomyelitis is similar to that of the disease in horses. In 1931, in California, Meyer[67] encountered 3 human cases with pathologic lesions similar to those found in horses, although the virus was not isolated and neutralizing antibodies were not demonstrated. During the next six years,

there was no record of outbreaks in man, although the viruses were widespread, as indicated by the occurrence of the disease in horses. There was some suggestion that sporadic cases occurred during this period.[68, 69] In the summers of 1937 and 1938, however, outbreaks of encephalitis occurred in California, North Dakota, Minnesota, Saskatchewan and Massachusetts, and an etiologic diagnosis was established by the isolation of both types of the equine virus and demonstration of specific neutralizing substances in the serums of patients.[5–8, 12, 48, 70–75] The epidemic in Massachusetts was due to the Eastern variety of virus; all the others were due to the Western type. One strain of the Eastern virus isolated from a fatal human case produced typical encephalomyelitis in the horse.[76]

During the last three summers, no epidemics have occurred in the East, but outbreaks of increasing severity have been reported in the Midwest and Far West,[15, 17, 18] culminating in the extensive outbreak during the past summer in the north central states and the adjoining provinces of Canada.[1] As pointed out above, both the Western equine and St. Louis viruses have been isolated in California, Colorado, North Dakota and Washington.[7, 14, 15, 17, 18, 68, 77] Thus far, the evidence indicates that the recent epidemic in the Dakotas and surrounding states and in Canada is due to the Western strain of equine virus,[78–80] although poliomyelitis probably coexists in certain areas. Sporadic subclinical and fatal infections have been reported in laboratory workers.[81–83]

Other Types of Encephalitis

Three other specific types of acute encephalitis have occurred in epidemic form, namely, Japanese B encephalitis, Australian X disease and the "forest-spring" encephalitis of Russia.

The Japanese disease has been recognized since 1871.[84, 85] It is caused by a specific virus,[35, 38, 86, 87] which is apparently related antigenically to, although not identical with, the St. Louis virus.[38, 88–90]

Australian X disease, or the so-called "mysterious disease," occurred in New South Wales in 1917 and 1918 and returned in milder form in 1922 and 1926.[91–94] It has not been seen since. Enough evidence was obtained, however, to show that the infectious agent was probably a virus, although the strain has been lost so that comparison with the other viruses in this group has been impossible.

Recent reports[95–98] have described a seasonal encephalitis that has existed in Russia for at least twenty-five years. It occurs in the spring, attacks primarily men laboring in the forest, and accordingly is known as "forest-spring" encephalitis. The etiologic agent is a virus that is distinct from that of St. Louis encephalitis but is antigenically related to the virus of Japanese B encephalitis. Differentiation is possible, however, by immunologic methods.

The virus of louping ill, under natural conditions, produces an encephalitis of sheep in Scotland, where no epidemics or even sporadic cases in man have been reported, although accidental laboratory infections have occurred.[99] The disease is of chief interest academically because of the similarity of the experimental infection to that produced by other viruses causing acute encephalitis.

The B virus was isolated from the central nervous system and spleen of a laboratory worker who had developed an acute ascending myelitis following the bite of a monkey.[100, 101] Apart from such accidental infection, this disease is unknown in man.

Lymphocytic choriomeningitis, a natural disease of mice, occurs sporadically in man.[102–105] The specific virus has been isolated from patients. The disease appears to be primarily a meningitis, but because of the lack of pathological data, the extent of involvement of the central nervous system in man is unknown.

Transmission and Host Reservoirs

The source and manner of spread of the viruses causing encephalitis in man presented a puzzling problem that has tested the ingenuity and imagination of a large number of investigators. Even in the earliest outbreaks, it became evident that individual contact did not explain the occurrence and spread of the infections. Certain aspects of the epidemics — seasonal occurrence, geographic distribution and related outbreaks in animals — suggested animal and avian host reservoirs and vector transmission. During the last few years, this concept has been substantiated to a considerable degree. In fact, for only two of the known virus encephalitides — poliomyelitis and Australian X disease — is evidence of potential animal reservoirs lacking, and vector transmission is possible with at least five of the viruses.

This advance has been achieved by the correlation of several types of data obtained by studying the following: the epidemiology; the susceptibility of domestic and wild animals and birds; the distribution of the virus in blood and tissues of experimentally or naturally infected animals and birds; the isolation of the virus from naturally infected animals and birds; the presence of neutralizing substances in the blood of

man and of wild and domestic animals and birds; the experimental transmission by vectors; and the isolation of the virus from naturally infected vectors and the transmission of disease by them to normal susceptible animals.

St. Louis Encephalitis

Studies of the 1933 outbreak in St. Louis did not reveal the mode of transmission,[3, 4] although, on reanalyzing the data, Casey and Broun[106] came to the conclusion that every known feature was common to that of a mosquito-borne disease. Although the virus was found only in the central nervous system of fatal cases,[31] it has been demonstrated in the blood of experimental animals.[107] Infection could be produced by intranasal inoculation, as well as by direct intracerebral injection.[32] Clinical signs of infection occurred in monkeys and mice, and possibly in mules,[4] but the other common laboratory animals were resistant. The virus was not found in mosquitoes collected in epidemic areas.[3] One species of anopheline mosquito became infected by biting a diseased animal,[108] but transmission was not accomplished.

Additional information then followed rapidly. The fact that mice could apparently be immunized by intranasal instillation of nasopharyngeal washings from patients[109] suggested that subinfective amounts of virus were present in the nasal secretions and that contact infection might therefore be possible. Wild mice were found to be susceptible,[110] and adult mice contracted the disease by eating infected, newly-born mice, suggesting a possible mode of transmission in nature.[111] The common mosquito, *Culex pipiens*, was able to take up the virus but not to transmit it.[112] Certain individual field and meadow mice were found to be susceptible to the St. Louis virus, whereas others were resistant[113]; this suggested that the latter had acquired immunity from natural infection or were carriers and hence potential reservoirs of the virus.

Because the serums of a significant number of wild and domestic animals and birds were found to be capable of neutralizing the St. Louis virus,[17, 18, 114] the possibility of previous infection was indicated. Inoculation of St. Louis virus intracerebrally into horses whose serums contained neutralizing antibodies resulted in no apparent illness, whereas animals whose serums did not contain antibodies developed an acute encephalitis, indistinguishable from that produced by the virus of equine encephalomyelitis.[115] During the course of this experimental disease, the infective agent was found in the nasal secretions but could not be detected in the blood. It seems unlikely, therefore, that transmission from the horse could be accomplished by blood-sucking insects. Since the virus is present in nasal secretions, transmission by contact or by mechanical vectors may be possible, with the nasopharynx as the portal of entry.

Finally, Hammon and his co-workers[116] reported the isolation of St. Louis virus from mosquitoes (*C. tarsalis*) collected from areas in which human encephalitis occurred. This insect may therefore be the vector, and several species of wild and domestic birds and mammals may be the host reservoirs; both horses and human beings may be only accidental victims. It remains to be determined, however, whether the virus is actually present in the blood of these animals and birds, whether it can be transmitted from them to susceptible hosts by mosquitoes, and whether or not contact produces infection. Until such data are available, the epidemiology of this disease will remain incomplete.

Equine Encephalomyelitis

Soon after the recognition of epidemics of equine encephalitis in horses, it was noted that the disease disappeared in the fall shortly after the first frost, which suggested the possibility that an insect vector might be involved. This suspicion was strengthened by Kelser's demonstration,[117] amply confirmed by others,[118–124] of the experimental transmission of the disease in the laboratory by mosquitoes. Studies of both the Western and Eastern strains of virus by many investigators[125–142] revealed the wide range of infectivity of the agents for animals and birds by several routes of injection. Furthermore, the virus could be detected in their bloods in the early stages of the disease.

On the basis of the epidemiology of the disease in horses in the eastern United States, TenBroeck, Hurst and Traub[143] considered birds as possible host reservoirs. This hypothesis was supported during the 1938 epidemic in the East by the isolation of the virus from the ring-necked pheasant[144, 145] and the pigeon,[146] and recently in the West from the prairie chicken.[78] Mosquitoes capable of transmitting the infection existed in these areas,[1, 124, 147] but numerous attempts to isolate the virus from mosquitoes collected during epidemic periods failed. More recently, however, neutralizing antibodies for the Western strain of equine virus were found in the serums of a number of wild and domestic birds and mammals in epidemic areas in the West,[114] and the virus was isolated from mosquitoes (*C. tarsalis*) collected in those areas.[116] Thus, it seems probable that mosquitoes are important vectors in transmitting equine encephalomyelitis among birds and ani-

mals, the primary hosts, as well as to man, a secondary host.

Outbreaks have been recorded, however, in an area that had been dry for months and absolutely free from mosquitoes for weeks before the appearance of the disease.[8] It is entirely possible that arthropod vectors, such as the tick, may be involved.[148, 149] Moreover, the Western strain of equine virus has recently been isolated from naturally infected *Triatoma sanguisuga*, commonly known as the assassin bug or the bloodsucking cone nose, and in one case the disease has been transmitted to guinea pigs[150] by this arthropod.

Other Types of Encephalitis

Considerable information is available regarding the host reservoirs and mode of transmission of certain other encephalitides of virus etiology. Japanese B encephalitis can be transmitted by mosquitoes (*C. pipiens*), but host reservoirs are not known, although monkeys, mice and sheep are susceptible to the virus.[38, 85, 86, 88, 90, 151, 152] The virus of the "forest-spring" encephalitis of Russia has been isolated from rodents in endemic areas and can be transmitted by ticks.[95–98] Little is known regarding Australian X disease except that the monkey, sheep, horse, calf and possibly guinea pig were shown to be susceptible. Louping ill is primarily a disease of sheep and is transmitted by the sheep tick, *Ixodes ricinus*.[153] No vectors are known for virus B encephalitis, which presumably is a disease of monkeys.[100, 101] Lymphocytic choriomeningitis is a natural disease of mice, but the virus has also been isolated from guinea pigs, monkeys and dogs, as well as from man,[154] and laboratory transmission has been effected by mosquitoes.[155]

Clinical and Pathological Aspects and Diagnosis

The acute encephalitides of virus etiology that occur epidemically are remarkably similar in their clinical aspects, so that in the present state of knowledge differentiation between them on this basis is not possible, except in cases of poliomyelitis.

St. Louis encephalitis[4, 18, 47, 156–158] and the Eastern[9, 70, 73, 74] and Western[1, 5, 7, 14, 15, 18, 68, 77, 82, 83, 159] types of equine encephalomyelitis have occurred epidemically in man in this country. Each of these diseases has appeared in midsummer or late summer. The onset of illness was usually abrupt, although in some patients a prodromal period occurred, characterized by a grippe-like syndrome of fever, malaise, muscle pains and so forth. Headache, fever, mental confusion and signs of meningeal irritation were outstanding features. In severe cases, drowsiness, tremors, convulsions and coma occurred early in the course, particularly in the younger age group. Jaundice was apparent in some cases.[18] Signs of involvement of the central nervous system varied considerably. Some showed only hyperactive reflexes, whereas others developed extensive paralyses which were usually spastic. Ocular manifestations were rare. The acute illness usually subsided in one or two weeks, and the majority of deaths occurred within the first week. Sequelas were rare in patients who recovered from St. Louis encephalitis,[157] but were frequent and often severe in those—particularly children—surviving equine encephalomyelitis.[68, 74, 77] The mortality was much higher with the Eastern type of equine encephalomyelitis than with either the Western or St. Louis type, which is in keeping with the greater virulence of the Eastern strain of equine virus.

Examination of the cerebrospinal fluid revealed elevated protein, normal sugar and a pleocytosis varying from 10 to 2000 cells per cubic millimeter. In general, the cell counts were lower, 50 to 250, and mononuclear cells predominated with St. Louis encephalitis, whereas the total counts were higher and polymorphonuclear cells predominated in the early stages with equine encephalomyelitis. Polymorphonuclear leukocytosis was found in the blood of some patients.

The pathologic changes in each of these varieties of encephalitis were localized chiefly in the central nervous system and were essentially similar.[7, 73, 74, 160–162] Edema, congestion, cellular infiltration about vessels and in the parenchyma, neuronal degeneration and neuronophagia were present. The process was diffuse, although the spinal cord was usually spared. Considerable parenchymal infiltration with polymorphonuclear leukocytes, arteritis and thrombosis of small arteries and arterioles were found in the brain and brain stem of fatal cases due to the Eastern strain of equine virus.[162]

Differential diagnosis is often difficult,[163] particularly in sporadic cases,[164] and a final etiologic diagnosis must be made with laboratory aid (Table 1). The Western strain of equine virus has been found in the blood[8, 75] and cerebrospinal fluid[82] early in the course of this disease. Each of the viruses has been isolated from the nervous tissue of fatal cases.[70–72, 78] Animals are usually employed for this purpose, although tissue culture may be a more sensitive method.[165] An etiologic diagnosis may also be made by the demonstration of neutralizing or complement-fixing antibodies in serums[27, 79, 80, 166, 167] or cerebrospinal fluid from

convalescents.[107] Neutralizing antibodies may be detected by the end of the first week after onset in some cases,[26, 107] but more frequently during the second and third weeks. The most reliable evidence is obtained when serums taken during the acute and convalescent stages show an increase in titer.

As mentioned earlier, encephalitis lethargica or von Economo's disease was a fairly definite clinical syndrome, which differed in many respects from the acute encephalitides just described. Following its appearance in 1916, the disease increased progressed for years, with remissions and relapses. The pathologic changes were inflammatory in nature and most prominent in the area of the basal ganglia. The presence of varying stages of inflammation and nerve-cell degeneration suggested persistence of an active process late in the course of the disease.[168, 169] The etiology was not established, in spite of extensive investigation, and it is therefore not possible to classify this syndrome as a virus disease.

Lymphocytic choriomeningitis is characterized chiefly by the signs and symptoms of meningeal

TABLE 1. *Certain Differential Features of the Encephalitides Occurring in Man in the United States.*

Type of Encephalitis	Season	Age	Onset	Course	Sequelas	Approximate Mortality	Cerebrospinal Fluid		Presence of Specific Virus			Presence of Circulating Antibodies
							White-cell count	Predominating cells	Blood	Cerebrospinal fluid	Central nervous system	
						%						
St. Louis	Late summer	Adults	Sudden	Acute	Rare	20	10–1000	Mononuclear	?	?	+	+
Eastern equine	Late summer	Children	Sudden	Acute	Frequent and severe	70	20–2000	Polymorphonuclear, early; mononuclear, late.	?	?	+	+
Western equine	Late summer	Any	Sudden	Acute	Frequent and severe	20	100–1000	Polymorphonuclear, early; mononuclear, late.	+	+	+	+
Encephalitis lethargica	Winter	Any	Sudden, gradual or not apparent	Chronic	Frequent and progressive	30	0–100	Mononuclear	0	0	0	0
Lymphocytic choriomeningitis	Any	Any	Sudden	Acute	Very rare	0	100–3000	Lymphocytes	+	+	?	+

to epidemic proportions, reaching a peak in 1924 and 1925 and declining during the next few years. New cases have been comparatively rare during the last decade. This form of the disease occurred in the winter and affected all age groups. The onset of acute symptoms and signs was sudden in some cases, gradual in others, and at times was unrecognized until the appearance of sequelas. Low-grade fever, minimal evidences of meningeal irritation, headache and, occasionally, somnolence were the chief early manifestations. The cerebrospinal fluid showed minimal changes — slight increase in protein and a count of 10 to 50 mononuclear cells — or none at all. The illness was ordinarily chronic and gradually progressive. Ocular paralyses, somnolence or drowsiness, emotional changes and, sometimes, paralyses occurred during the succeeding weeks and months. Emotional and mental deterioration and Parkinson's syndrome were usually characteristic features. In some cases, complete recovery occurred; in others, the disease irritation, although drowsiness and coma may occur. Other conditions that must be considered in differential diagnosis are acute meningitis, chronic meningitis (tuberculous and syphilitic), the post-infection encephalitides and other demyelinating processes.

TREATMENT

Treatment of all the encephalitides is chiefly symptomatic at present. Lumbar puncture and the intravenous administration of hypertonic dextrose solutions are of value in relieving increased intracranial pressure. Sedation and correction of dehydration should be carried out when indicated. Chemotherapy with sulfonamides is of no value, except for the prevention or treatment of complications, such as bronchopneumonia.

Specific antiserum has been employed in horses and experimental animals, with conflicting results.[170–172] Convalescent human serum was of no demonstrable therapeutic value during the St.

Louis epidemic.[173] As Hammon[18] has pointed out, specific therapeutic antiserums are of no avail at the present time because a sufficiently early etiologic diagnosis cannot be made. Rosenow and his co-workers[4, 174] have reported studies indicating that streptococci are etiologic agents of the various types of encephalitis. On the basis of this work, they have advocated antistreptococcus serum and streptococcal vaccines for therapy and prophylaxis. Their results have not been confirmed by other investigators.[4]

Prevention

Three methods of attack now appear to be applicable to the prevention of epidemics of encephalitis in this country: extermination of host reservoirs, extermination of vectors and immunization of susceptible hosts. The evidence now available indicates that the natural reservoirs may be so widely diverse in animals and birds[78, 114, 144–146] as to make their extinction impossible. Measures to control mosquitoes and other insects are feasible in many populated areas of the country, and should be carried out where applicable. Immunity to equine encephalomyelitis can be produced in susceptible hosts by vaccines containing the specific virus, which has been killed by formalin or ultraviolet light.[175–179] Such vaccines have been used in horses, with apparently good results.[63, 65, 179] Purified vaccine[180–182] is now available and has been employed in human beings with only minor reactions.[183, 184] Its use seems to be desirable in laboratory workers and in those persons in endemic areas whose occupations offer frequent opportunity for infection. Animals have been immunized against St. Louis encephalitis virus by the use of living virus,[185, 186] but vaccines that can safely be used in man are not yet available.

Further investigation of the problems of prevention is essential, because of the military activities and concentration of men in training camps situated in endemic areas.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27521

PRESENTATION OF CASE

First admission. A thirty-year-old Italian housewife was admitted to the hospital because of swelling of the legs and abdomen for three weeks.

About six years before entry, the patient had a slight sore throat, followed shortly by painful swelling of her joints. She remained in bed for three months, because a local physician thought "her heart was affected." Her tonsils were removed, and she remained well until four years before entry when again she had "rheumatism," and stayed in bed for two or three months. At this time, some abscessed teeth were found and removed. Following this illness, there was insidious onset of shortness of breath. Dependent edema appeared about eight months before entry, and was not relieved by theocin, which was given by the patient's physician.

Her past and family histories were not of importance. She had an eight-year-old son.

On examination, the patient appeared well developed but poorly nourished; she was markedly dyspneic, with cold extremities and circumoral cyanosis. The neck veins were distended. The heart was enlarged 4 cm. to the right and 12 cm. to the left of the midline, and fibrillated at a rate of about 156, only about half the beats coming through at the wrist. There was a prominent precordial heave, and a diffuse systolic murmur at the apex, with a mid-diastolic murmur and thrill. Each lung field exhibited basal rales. The liver border was tender, and lay three finger-breadths below the costal margin. Free fluid was present in the lower abdomen, and the sacral tissues and lower extremities were quite edematous.

The temperature was 97°F., the pulse 92, and the respirations 25.

Examination of the blood showed a red-cell count of 6,010,000 with 90 per cent hemoglobin, and a white-cell count of 7400 with 62 per cent polymorphonuclears. The blood Hinton reaction was negative. The urine showed a slight trace of albumin, and contained many hyaline casts and a few white blood cells per high-power field. An electrocardiogram confirmed the diagnosis of auricular fibrillation, and demonstrated prominent right-axis deviation, with inversion of T waves in Leads 2 and 3. The vital capacity was 1200 cc. The basal metabolic rate was -16 per cent.

The patient was given diuretics and Southey tubes, with improvement in her condition. In the fourth hospital week, total thyroidectomy was performed. Tetany developed after the operation, the blood calcium falling to 8 mg. and the blood phosphorus rising to 6 mg. per 100 cc. Following recovery, the patient was discharged at the end of the second hospital month on digitalis and calcium chloride. By this time, the basal metabolic rate had fallen to -21 per cent, the vital capacity had improved to 1450 cc., and the pulse had become regular at 70.

Second admission (one year later). The patient was readmitted because of pain in the back and because of recurrence of her dyspnea and edema. She had remained in bed on digitalis. Nine hours before re-entry, she experienced a sudden, sharp pain in her left flank and soon afterward passed a small amount of bloody urine. She was found to be in congestive failure, the condition being little changed from that observed on the first entry, except for the presence of hematuria, which persisted throughout the two weeks of her hospital stay, and except for slight evidence of hypothyroidism — dry skin, a basal metabolic rate of -27 per cent, a blood pressure of 110 systolic, 93 diastolic, and a pulse of 60. The nonprotein nitrogen was 47 mg. per 100 cc. Three and a half liters of dark yellow ascitic fluid was removed by tap. The patient was given Salyrgan and discharged improved.

Third admission (four months later). The patient was readmitted with her usual complaints of dyspnea and edema, to be discharged two weeks later after the usual diuresis. The heart rhythm was regular, and the urine was normal except for the presence of albumin.

Fourth admission (three and a half years later). During the preceding four years, the patient had been able to do light housework, remaining fairly well until two and a half months before readmission. She then had a cold, accompanied by pain in the chest and migratory swelling of the fingers, shoulders and knees. After a week, the dyspnea, orthopnea and edema reappeared. Re-examination showed a rumbling apical diastolic murmur in addition to the old systolic murmur. The heart was again in fibrillation, and the blood pressure had risen to 115 systolic, 70 diastolic. The white-cell count ranged from 13,000 to 15,000, with 76 per cent polymorphonuclears. The sedimentation rate was elevated to 1.5. The blood

calcium was 9.8 mg., and the blood phosphorus 5.3 mg. per 100 cc. The urine showed a ++++ test for albumin and contained many white blood cells, with a few casts and red blood cells per high-power field. On discharge, after two months of bed rest, there were persistent signs of active disease in the joints.

Fifth admission (six months later). The patient returned to the hospital because of a return of congestive failure. She was discharged improved, after a month.

Sixth admission (four months later). The patient was once more admitted because of decompensation. The basal metabolic rate had risen to normal. The calcium and phosphorus levels of the blood were each 7.1 mg. per 100 cc. She was given AT-10 (the calcinosis factor of previtamin D), and elevation of the blood-calcium level to 12 mg. per 100 cc. was attained. A colon-bacillus infection of the urine was discovered and treated satisfactorily with mandelic acid.

Seventh admission (two weeks later). The patient received the usual treatment for recurrent decompensation, to be discharged after a month.

Eighth admission (fifteen months later). The patient was hospitalized for a day because of "numbness" in the hands and face, and a "tight feeling" in the abdomen. The Chvostek and Trousseau signs were markedly positive, and she appeared to be in incipient tetany. The symptoms were relieved by an increase in the daily ration of calcium lactate.

Final admission (one month later — seven and a half years after her initial entry). The patient was readmitted because of progressive dyspnea. She had been leading a bed-chair existence. Two days before entry, she began to have considerable pain in the abdomen.

On examination, she appeared acutely ill, severely dyspneic and orthopneic, and quite cyanotic. The heart was enormous, beating irregularly in slow, coupled rhythm. Murmurs were present as before. Rales extended half way to the angle of the scapula on the right. The liver was several centimeters below the level of the umbilicus and was acutely tender. There was little peripheral edema.

The temperature was 99°F., the pulse 40, and the respirations 18. The blood pressure was 120 systolic, 70 diastolic.

Examination of the blood showed an elevation of the white-cell count to 15,400. The blood calcium was 8 mg., and the phosphorus 14 mg. per 100 cc. Other laboratory studies were much as before.

The temperature rose to 101.2°F., and the pulse to 100. Death occurred suddenly and unexpectedly on the third hospital day.

Differential Diagnosis

Dr. Richard J. Clark: This patient was quite evidently one of that group subjected to total thyroidectomy for the treatment of heart failure a few years ago. Six years before the first admission, she had acute rheumatic fever, with cardiac involvement aggravated by a second bout of infection two years later, when she first showed symptoms of congestive heart failure that progressed up to her entry into the hospital. At entry, she was in acute congestive failure, with cardiac enlargement and auricular fibrillation. She showed evidence of mitral damage, with an apical systolic and mid-diastolic murmur and thrill. The electrocardiogram at entry was consistent with mitral disease and right ventricular hypertrophy. The temperature and white-cell count afforded no evidence of active rheumatic infection at this time. The findings in the urine were consistent with those of congestive heart failure.

The patient's condition improved with diuretics and Southey tubes. Although the basal metabolic rate was −16 per cent, a total thyroidectomy was performed. This must have been one of the early cases in the series, because later it was believed that the presence of an initially low basal metabolic rate gives a relatively poorer outlook for improvement with this type of therapy. The patient developed clinical and laboratory evidence of hypoparathyroidism after the operation, but otherwise made a good convalescence. I note that four weeks after total thyroidectomy the basal metabolic rate had fallen only to −21 per cent, which is not much of a drop from the preoperative rate of −16.

One year later, the patient re-entered the hospital with recurring congestive failure and also pain in the left flank followed by bloody urine. Evidently she had experienced what is not uncommon in the disease complex — a renal infarct. The nonprotein nitrogen and the diastolic blood pressure were elevated. This gives strong evidence of frank renal disease. The basal metabolic rate was only −27 per cent. Apparently, no thyroid medication was given. If a total thyroidectomy was actually performed, a rate considerably lower than this would have been expected at this time.

The third admission, four months later, gives us little added data. The patient was still in failure. Her rhythm at the moment was regular.

On the fourth admission, she reported an improved state. For four years, she had been able

to do light housework, up to the evident development of recurrent active rheumatic fever following a respiratory infection. The mitral stenosis was apparently becoming more marked, with a rumbling mitral diastolic murmur. Laboratory studies confirmed the presence of active infection. The urine showed many white cells in addition to albumin, casts and blood cells. In spite of this, the blood pressure was relatively low.

Six months later, the patient re-entered the hospital with congestive failure.

On the sixth admission, four months later, she was again in failure. Surprisingly, there was a normal metabolic rate. There is still no mention of thyroid medication. This strongly suggests that the supposedly totally ablated thyroid gland had regenerated, but she still had hypoparathyroidism. She showed a definite colon-bacillus infection of the urine.

The seventh admission was for further congestive failure. The eighth admission was for treatment of incipient tetany.

The final entry (seven and a half years after the initial entry) was for further congestive failure. The patient had considerable abdominal pain, just where we are not told, but there is little to correlate this with, except for the enlarged, tender liver. She had a rise in temperature and white-cell count. There is no positive evidence on which to say whether this was recurrent rheumatic infection or terminal pulmonary infection, or even urinary infection. The heart had become "enormous." Slow irregular rhythm with coupling indicates a diseased myocardium, if not made toxic with digitalis. We have no details regarding the sudden and unexpected death. A massive pulmonary embolus may have occurred, but there is no positive evidence for this. The patient may very well have had acute cardiac dilatation and standstill, with acute pulmonary edema.

There can be little doubt that this patient had primarily rheumatic heart disease, with chronically recurrent rheumatic fever. She must have developed an extreme degree of mitral stenosis. There was never any evidence of aortic involvement. The tricuspid valve was undoubtedly dilated and incompetent. We may wonder about tricuspid stenosis, but cannot make this as a positive diagnosis. In the treatment of the congestive failure, total thyroidectomy was given a trial. As we read this protocol, we can hardly believe that this procedure accomplished a great deal for the patient, unless it were in prolonging a rather miserable life. I believe we shall find that a full ablation of the gland was not done and that regeneration of functional tissue took place. The alternate to this may be that aberrant thyroid tissue was present and subsequently hypertrophied. A large part of the parathyroid tissue must have been removed at operation, resulting in a persistent hypoparathyroidism; we may find a scarred portion of one gland remaining. All the visceral organs must have shown an extreme degree of chronic passive congestion from the years of heart failure. We may wonder about cardiac cirrhosis, but chronic ascites toward the end was hardly significant enough to warrant this diagnosis, and the liver remained enlarged. We have evidence for at least one old embolic scar in the left kidney, and similar areas of infarction may have been found in the other organs. I am left wondering about the kidneys. In the later entries, further information regarding nonprotein nitrogen and urinary findings is not given. We know that there had been a urinary infection. Undoubtedly, the kidneys, like the liver, showed an extreme degree of chronic passive congestion, and it is possible that they showed a superimposed chronic pyelonephritis. There may well also have been a focal nephritis.

Clinical Diagnoses

Rheumatic heart disease, with mitral stenosis and regurgitation.
Tricuspid regurgitation?
Hypothyroidism.
Hypoparathyroidism?
Auricular fibrillation.

Dr. Clark's Diagnoses

Rheumatic heart disease: mitral stenosis; aortic and tricuspid involvement (?).
Cardiac cirrhosis?
Chronic passive congestion.
Hypoparathyroidism.
Regeneration of thyroid gland.
Pyelonephritis?

Anatomical Diagnoses

Rheumatic heart disease: mitral stenosis and regurgitation; aortic stenosis, slight; tricuspid regurgitation; pulmonary endocarditis, slight; adhesive pericarditis.
Chronic passive congestion.
Cardiac cirrhosis of the liver.
Hydrothorax, bilateral, slight.
Ascites.
Hemorrhagic enterocolitis, acute.
Partial regeneration and hyperplasia of thyroid gland.
Partial removal of thyroid and parathyroid glands.

Pathological Discussion

Dr. Tracy B. Mallory: The essential pathologic lesion in this case was, of course, rheumatic heart disease. As Dr. Clark predicted, there was a high grade of mitral stenosis, and, as he suspected but could not prove, the aortic and tricuspid valves were also involved. There was enough interadherence of the aortic cusp to have produced a slight but definite stenosis, and the chordae of the tricuspid valve were so shortened that there must have been regurgitation. A minimal scarring, without functional deformity, was also noted on the pulmonary valve. Further evidence of a pancarditis was an almost complete fibrous obliteration of the pericardial cavity. Neither in the valves nor in the myocardium could we find any evidence of acute rheumatic infection.

Another suspicion of Dr. Clark's was likewise confirmed. The liver was small, and its surface very finely pebbled; it cut with definitely increased resistance. On microscopic examination, distinct fibrosis of the centers of the lobules was apparent, in addition to the evidence of severe passive congestion. So that the diagnosis of cardiac cirrhosis was confirmed.

The lungs showed little except chronic passive congestion, and the terminal episode proved to have been a diffuse hemorrhagic enterocolitis, which was entirely unexpected. The kidneys were surprisingly normal. They were of course, slightly swollen and congested, but there was no evidence of pyelonephritis, and we did not find any scar of a healed infarct. As Dr. Clark guessed, the thyroidectomy had not been total. A nodule that weighed between 2 and 3 gm. and showed on microscopic examination intense hyperplasia had regenerated. In a search for parathyroid glands, a small fragment of accessory thyroid tissue was found, which was likewise hyperplastic. No parathyroid gland could be identified.

CASE 27522

Presentation of Case

A fifty-one-year-old Italian laborer was transferred to the Emergency Ward from another hospital because of coma and increasing neurologic signs of thirty-six hours' duration.

Five weeks before admission, the patient became flushed, had chills, began to cough, and complained of pain in the left lower chest. He remained in bed for three days, but did not improve and entered a local hospital, where examination showed crackling rales over the upper left chest, with dullness to flatness below the level of the left fourth rib. There was marked bronchovesicular breathing in the right chest. An x-ray film showed consolidation in the left lower lobe of the lung. The head and abdomen were normal.

The patient was treated with sulfathiazole, but responded poorly. Subsequent x-ray films showed persistent consolidation in the left base, and an apparent left interlobar mass, which became progressively more prominent. Several chest taps failed to reveal fluid or pus. The temperature spiked between 101 and 105°F. (rectal) for two and a half weeks. Following a four-day course of sulfapyridine, the temperature returned to normal, and there was general improvement in the patient's condition.

Five weeks after onset of the illness, while still in the local hospital, the patient suddenly became apathetic, listless and unresponsive. He developed sphincter incontinence, and in the course of thirty-six hours lapsed into deep coma.

The family history was noncontributory. The patient was a chronic alcoholic.

Physical examination showed a comatose, apparently moribund man who was breathing stertorously but regularly. There was no cyanosis. A leathery rub was heard in the left axilla, and there were scattered rales in the left base. Dullness was evident posteriorly on the left at the level of the fifth and sixth ribs, medial to the scapula. The liver edge seemed firm and smooth and was two fingerbreadths beneath the costal margin. The pupils were round but unequal, and reacted to light. The fundi showed full retinal veins, with initial blurring of the disks. There was a suggestive left central facial weakness. The head was held tilted and rotated to the left, with marked rigidity of the neck. All extremities were hypertonic, the right arm more than the left. The tendon reflexes were exaggerated bilaterally although more markedly so on the right. The abdominal reflexes were absent, and the Babinski reflex was positive on both sides.

The heart sounds were rapid and distant. The pulse was 110, the temperature 106°F., and the respirations 40.

Examination of the blood showed a red-cell count of 3,050,000 with a hemoglobin of 50 per cent, and a white-cell count of 21,600 with 93 per cent polymorphonuclears. The urine showed a specific gravity of 1.014, with a +++ test for albumin, no sugar, and only occasional white cells in the sediment. The nonprotein nitrogen of the blood serum was 20 mg. per 100 cc.

A lumbar puncture gave 6 cc. of turbid, later blood-tinged fluid, the pressure falling from 155

to 125 mm. of water. The respiratory and pulse oscillations were normal. The fluid showed a white-cell count of 4670, with polymorphonuclear leukocytes predominating. Gram-positive cocci in pairs and chains appeared on smear. Puncture of the left chest in the fifth interspace, 10 cm. lateral to the spinous process, yielded 45 cc. of sanguinopurulent fluid.

A roentgenogram of the chest showed homogeneous density obliterating the left side of the diaphragm, rising to the fourth rib posteriorly in a thin band. The heart was not displaced. A roentgenogram of the skull was normal.

The patient was continued on sulfapyridine, and a blood level of 13 mg. per 100 cc. was obtained. He was given repeated intravenous fluids and oxygen therapy.

Death occurred on the third hospital day, five and a half weeks after onset of the illness.

225
41

Differential Diagnosis

Dr. Augustus S. Rose: The cause of death in this case was clearly an intracranial infectious process. Meningitis was definitely established, as was the intrapleural infection from which the meningitis ultimately arose. The neurologic problem is therefore confined to the question of the coexistence of a brain abscess.

The terminal illness began with fever, chills, cough and pain in the chest, and physical and x-ray examinations confirmed the suspicion of lobar pneumonia. The consolidation, however, did not clear, and for a time, the patient responded poorly to clinical therapy. At this time, empyema, which was unquestionably present, was suspected, but fluid was not obtained by chest tap. Two and a half weeks later, while apparently convalescing, the patient suddenly became semicomatose, lost sphincter control and grew progressively worse until death three days later.

We are not told of the symptoms that he must have had during the two weeks between the two acute phases of his illness. But thirty-six hours after the onset of coma, physical examination and, indeed, a chest tap revealed the persistence of the empyema. Neurologic examination showed a stiff neck, unequal pupils, distended retinal veins, with a question of early papilledema, a suggestive left central facial weakness, unequal hyperactive reflexes and bilaterally positive Babinski signs. Lumbar puncture showed turbid, blood-tinged spinal fluid, with a white-cell count of 4600 cells and a normal pressure (155 mm. of water). A smear of the fluid showed gram-positive cocci in pairs and chains. The sugar determination would be of interest, but is unnecessary.

On the basis of these facts, we can say the patient had empyema of the left pleura and pneumococcal meningitis. However, does pneumococcal meningitis explain the total picture? Was there a brain abscess that ruptured into a ventricle?

Pneumococcal meningitis may be one of the most fulminating of meningeal infections. Not infrequently, it is ushered in by a convulsion and coma, and if the infection is untreated, death may follow in a day or two. More commonly, however, headache, chills and apathy precede the more dramatic symptoms by some hours. Neurologic signs, as in this case, may also appear in meningitis, because of degenerative changes in the cells of the cortex and brain stem, secondary to the overlying exudate and infection. There is room for doubt whether such widespread damage would occur in thirty-six hours as to produce the signs exhibited by this patient when the spinal-fluid pressure was normal. The pressure is almost universally elevated in severe meningitis. The absence of increased pressure in this case requires explanation. It is also unusual to find blood-tinged spinal fluid in uncomplicated meningitis.

These objections to meningitis (sudden onset, many neurologic signs, normal spinal-fluid pressure and blood-tinged spinal fluid) can be met by the diagnosis of one or more metastatic brain abscesses, with rupture of one into a lateral ventricle. It is possible that a bacteremia occurred during the first or second week of the illness, while the temperature was spiking. The advancing pulmonary infection could have overshadowed symptoms referable to the head. If the cerebral lesion had been located near the ventricular wall, dramatic neurologic signs would not necessarily have developed. Furthermore, it is a frequent clinical observation that a brain abscess may attain considerable size before the development of increased intracranial pressure. The rupture of an abscess into a ventricle almost invariably changes a relatively benign localized infection into a sudden, overwhelmingly malignant one.

Clinical Diagnoses

Pneumonia.
Empyema.
Brain abscess.
Meningitis.

Dr. Rose's Diagnoses

Empyema, left pleura.
Pneumococcal meningitis.
Brain abscess, ruptured.

Anatomical Diagnoses

Bacterial endocarditis, aortic valve.
Multiple infarcts of brain and spleen.
Meningitis.
Encapsulated empyema.
Lobar pneumonia, acute.
Cirrhosis of the liver, ? alcoholic.

Pathological Discussion

Dr. Charles S. Kubik: Dr. Rose, I thought, was about to make the correct diagnosis when he called attention to the signs of multiple cerebral lesions and to the blood-tinged spinal fluid. These features seemed to bother him: he implied that they did not fit in too well with his diagnoses, and I should agree that focal signs would be very unusual in acute meningitis, particularly early in the course of the illness. In our cases of abscess rupturing into the ventricle, the white-cell counts in the spinal fluid have been very high, from 20,000 to 40,000, the reason being that the cerebrospinal fluid has been flooded with the purulent contents of the abscess.

In this case, there was visible subarachnoid exudate on the convex surfaces of the brain. The right middle cerebral artery was occluded by an embolus, and there was softening in the region supplied by it. A small infarct, 0.5 to 1 cm. in diameter, was found in the central portion of the base of the pons. This may explain why signs of pyramidal-tract disease were present on both sides. Microscopic examination revealed, in addition to the findings already mentioned, many tiny infarcts — most of them not more than 0.2 mm. in diameter — in the cerebral cortex and subcortical white matter. Findings such as these are observed in acute and subacute bacterial endocarditis in a large proportion of cases. Given a subarachnoid exudate, often patchy, usually with a fairly large percentage of polymorphonuclear cells, with small subarachnoid hemorrhages and the tiny infarcts mentioned above, the diagnosis can be made from the cerebral lesion alone. Large infarcts may or may not be present. The meningitis, obviously, is due to infected emboli arrested in the small arteries in the subarachnoid space. Infection extends through the vessel wall, and a "mycotic aneurysm" or weak spot may result and, later, leak or rupture. Mycotic aneurysms may also involve fairly large branches and may cause extensive subarachnoid bleeding. In cases with meningeal involvement, the clinical manifestations are those of a meningitis. Focal signs may or may not be present, depending on the extent and location of cerebral infarction. In the subacute cases, there may not be more than a hundred or a few hundred cells in the spinal fluid, which usually also contains red blood cells and is often xanthochromic. Also, in the subacute cases, organisms may not be found in smears or by culturing the fluid. There is often a remission of symptoms, and this was observed even before the days of chemotherapy. This clinical picture, with a swinging temperature, may even provide the clue to the diagnosis when heart findings are inconclusive and blood cultures are negative. It should be added that cerebral embolism and infarction, without any meningeal reaction, may also occur.

Dr. Tracy B. Mallory: The bacterial endocarditis, which Dr. Kubik was able to predict from the cerebral findings, was quite obvious. All three cusps of the aortic valve presented large, shaggy vegetations, ranging from 0.5 to 1 cm. in size. We were not able to make out any underlying deformity of the valve to suggest previous rheumatic infection. The mitral valve was entirely normal. Numerous cocci could be seen in the vegetation on microscopic examination but were, of course, morphologically unidentifiable. The post-mortem blood culture showed a mixed growth of *Staphylococcus albus* and an alpha-hemolytic streptococcus. No blood cultures were taken during life to check on these results. An encapsulated empyema was found in the left pleural cavity, and cultures from this yielded, as one would expect, pneumococci. There was a fresh terminal pneumonia of the left upper lobe.

The liver showed a well-marked cirrhosis, presumably correlating with the long alcoholic history, although the lesion was so inactive that no typical alcoholic hyalin could be identified. The spleen was quite large, weighing 625 gm., probably in part because of portal congestion behind the cirrhotic liver and certainly in part because of the bacterial endocarditis. It contained numerous infarcts of varying age. The kidneys showed no gross infarct, but microscopic evidence of embolic glomerulonephritis.

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225
41

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1942

It would be a mere meaningless repetition of a time-worn phrase to wish our readers, at this juncture, a happy and a prosperous New Year. There is no reason to believe that the year 1942 will be particularly happy in the usual gay meaning of the term, or especially prosperous, except as we may seize on the occasion to take arms against outrageous fortune and make our enterprises prosper.

Rather, at the beginning of next year we should form resolutions: to strip for the action that is ahead, to strengthen our own moral fiber and that of those about us, to banish fears and doubts and to be resolute. There will be dark days in the months to come, — days of discouragement, of depression, of sorrow, — but let there be no days of despair. The sands of democracy are far from running out, and the eventual reward of courage will be victory.

And may the faith of those peoples who have hitherto suffered be as great as that of Jeremiah, who, prophet of doom though he was, and imprisoned by the Chaldeans who were hammering at the gates of Jerusalem, gave proof of his belief in the ultimate rehabilitation of the nation by purchasing a plot of ground in the ancestral land of his family.

> Thus saith the Lord of hosts, the God of Israel: Take these evidences, this evidence of the purchase, both which is sealed, and this evidence which is open; and put them in an earthen vessel, that they may continue many days.
>
> For thus saith the Lord of hosts, the God of Israel; Houses and fields and vineyards shall be possessed again in this land.
>
> *Jeremiah* 32:14 and 15.

STANDARDS OF HEALTH

The span of a man's life during the Middle Ages is said to have been less than one third of what it is today, chiefly because of the ravages of disease and, to a less extent, of the effects of war. During more recent times, the mortality of soldiers whose country was at war was greater from disease than it was from injuries at the hands of the enemy. It is said that during World War I far more aviators died in action because of minor or serious defects inherent within themselves prior to enlistment than because of wounds inflicted by their antagonists. With World War II now entering its third year and with the United States — one of the great nations of the earth — an active participant in this struggle against tyranny and barbarism, physicians must consider not only the health of the Nation as a whole but that of the soldiers who will be called to defend their country. President Roosevelt has stressed the need of rehabilitation, and many philanthropic and medical organizations are greatly interested in this most important aspect of the Nation's welfare. On the other hand, careful regulations concerning the physical standards for the various branches of the United States Army and Navy have been drawn up with the purpose that life and matériel may be

conserved. These standards are necessarily high. It is possible that they should be still higher. In any event, the average physician is not familiar with them. He should be, for to him may fall the task of preliminary examination of applicants for one or another branch of the Army or Navy, and on him devolves the task of preventing or correcting, if possible, the defects in selectees or such applicants that disqualify for full military service. In this respect, two articles in this issue of the *Journal*, which deal with the cardiovascular standards for the United States Army and the general physical standards for its aviation cadets, are of particular interest. These standards should even be attained in civilian life, and they could be if the average physician were conversant with them. A better and stronger nation would result—come what may.

"Health is the second blessing that we mortals are capable of, a blessing that money cannot buy"—but wisdom and knowledge may.

MEDICAL EPONYM

Loeffler's Medium

The description of the culture medium that still bears his name occurs on page 461 of the monograph by Friedrich August Johann Loeffler (1852–1915), of Berlin, "Untersuchungen über die Bedeutung der Mikroorganismen für die Entstehung der Diphtherie beim Menschen, bei der Taube und beim Kalbe [Studies in the Significance of Micro-organisms in the Occurrence of Diphtheria in Man, in the Pigeon and in the Calf]," which was published in *Mittheilungen aus dem kaiserlichen Gesundheitsamte* (**2**: 421–499, 1884). A portion of the translation follows:

> When the bacilli were sown on the above-mentioned coagulated mixture of 3 parts of calves' or sheep's blood serum and 1 part of neutralized veal broth to which had been added peptone, 1 per cent, glucose, 1 per cent, and sodium chloride, 0.5 per cent, the organisms grew so luxuriantly that at the end of two days there was a whitish coat nearly 1 mm. thick over the surface of the serum, and single colonies had attained an average size of 0.5 cm. In all subsequent trials, therefore, this broth-peptone-glucose serum alone was used as a nutritive base.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Fatal Suppurative Uterine Infection and Peritonitis Following Self-Induced Abortion

A twenty-six-year-old unmarried woman was seen at home by her private physician and immediately sent into the hospital. She had passed a fetus five hours previously, and was thought to have been about three months pregnant. Since this was a medicolegal case, the past history was not complete. The patient was reported to have had an illegitimate pregnancy at term three years before the present episode. She was of subnormal mentality, and there was no history of illnesses of any sort.

On entry to the hospital, she had a foul lochia, a subnormal temperature, a pulse of 100 and respirations of 32. Under spinal anesthesia, the patient was curetted, and the uterus swabbed out with iodine. She remained in the hospital only three days and left against advice. During the hospital stay, the temperature did not go above normal.

Two and a half weeks later, she was referred to another hospital by another physician because of acute generalized abdominal pain and vomiting of three days' duration. Examination showed the abdomen to be generally tender, spastic and distended. There was no record of the temperature and pulse, but both were presumably elevated. Blood culture showed a staphylococcus. Sulfanilamide therapy, which had been started, was stopped after the report of the blood culture. The patient died two weeks after entry. Autopsy revealed a septic uterus and an acute suppurative generalized peritonitis.

Comment. There is little question that this was a self-induced abortion. This patient was described as being mentally subnormal. Pregnancy in this class of person is a great social problem; abortion is not frequent—much oftener these pregnancies go to term and complicate the social and economic problem for the state.

Although the patient herself was responsible for this death, the treatment that she received on entering the hospital is open to criticism. Conservatism in the handling of all septic abortions

*A series of selected case histories by members of the section have been published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, *Secretary*, 330 Dartmouth Street, Boston.

should be followed; this means leaving the uterus absolutely alone, except in the face of hemorrhage. In this case, the curettage was done not because of hemorrhage but because the patient was known to have aborted and still had a foul-smelling lochia. Since no temperature reaction followed this intrauterine manipulation, it may well be that the curettage did no appreciable harm, and it is barely possible that had this patient stayed in the hospital, the fatal outcome might have been prevented. In view of the subsequent history and the autopsy findings, sepsis was present in spite of the normal temperature when the patient went home. The diagnosis of peritonitis was so apparent when she entered the second hospital that only conservative treatment was applicable. It would be very helpful to the medical profession if the medical examiners were adamant in performing autopsies in all cases of maternal death that come under their jurisdiction.

If hemorrhage is a complication of septic abortion, it must be controlled, and the retained products, whose presence in the uterus is the cause of the hemorrhage, must be removed. The removal of such products should be done with the greatest care, preferably with the finger and not the curet, and the uterus should be packed to control further bleeding. Acute hemorrhage should be treated by transfusion, and in all septic abortions cultures from the uterus and blood stream should be taken and intelligent chemotherapy instituted. But in the absence of hemorrhage, the uterus should be left alone.

DEATHS

DUFFY — James J. Duffy, M.D., of New York City, died recently. He was in his fiftieth year.

Born in Webster, Massachusetts, Dr. Duffy received his degree from Harvard Medical School in 1919. He was a former member of the Massachusetts Medical Society.

FLEMING — Peter J. Fleming, M.D. of Jamaica Plain, died December 15. He was in sixty-seventh year.

Dr. Fleming received his degree from the University of Western Ontario Medical School in 1902. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

MANNING — Arthur F. Manning, M.D., of Waltham, died December 12. He was in his fortieth year.

Dr. Manning received his degree from Harvard Medical School in 1928. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

MARTIN — Archibald H. Martin, M.D., of Lynn, died December 13. He was in his seventieth year.

Born in Manchester, New Hampshire, Dr. Martin received his degree from the College of Physicians and Surgeons, Boston, in 1896. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a daughter and a son.

DEFENSE ACTIVITIES

CIVILIAN DEFENSE

Training of Volunteer Nurses' Aides

The national emergency has brought about a shortage of nurses in hospitals, clinics, public-health and field nursing agencies. To relieve this situation, which is likely to grow more acute with the expansion of military establishments and of plans for civilian defense, the American Red Cross and the Office of Civilian Defense have jointly undertaken a project to train volunteer nurses' aides. With such assistance, graduate nurses may extend their services to many more persons. The volunteer aides will work under supervision of a nurse and are being trained for certain nontechnical tasks in order that graduate nurses may be released for the highly technical duties they alone are qualified to perform.

The local chief of emergency medical service and the local office of civilian defense in communities where the training program is undertaken have definite responsibilities listed as follows by the national headquarters of the Office of Civilian Defense:

(1) To assist the local Red Cross chapter and the Civilian Defense Volunteer Office in recruiting and enrolling desirable applicants for training.

(2) To assist local chapters to conclude arrangements with appropriate general hospitals to serve as training centers.

(3) To assist the local Red Cross chapter in organizing and maintaining a placement service so that volunteer nurses' aides may continue to serve and to accumulate experience.

(4) To reassign volunteer nurses' aides to emergency duty if the need should arise.

The American Red Cross, in collaboration with the Medical Division of the Office of Civilian Defense, has revised its standard course of instruction for volunteer nurses' aides with reference to needs that may develop during the period of the national emergency. The standard course was instituted in July, 1940, an outgrowth of volunteer services that have been sponsored by the Red Cross since World War I. The first half of the course, consisting of lectures and demonstrations, is given in a Red Cross chapter house or some other suitable place. The second half is given in a hospital selected by the American Red Cross and the Office of Civilian Defense as a training center under strict supervision.

Nurses' aides are to work under supervision of a nurse at all times, never independently, the instructions point out. Moreover, they must agree to serve without remuneration and in time of national peril must be prepared to serve whenever and for as long a period as needed. Authorized duties for the nurses' aides have been outlined in the Red Cross publication, *Chapter Organization and Administration of Red Cross Volunteer Nurses' Aide Corps*. These duties are of course subject to approval of individual institutions. In hospitals they may, among other activities, make beds, take care of personal belong-

ings of patients, take care of rubber goods, clean dressing trays, take care of linen closets, feed helpless patients, take patients to and from treatment rooms, help with admission and discharge of patients and care for ambulatory patients. In dispensaries and clinics the aides may serve as interpreters in foreign languages, interpret clinic rules and instructions to patients, help weigh and measure, undress and dress children, assist in taking physicians' notes, help with inventories, clean and put away instruments and help put rooms in order after clinics. In community health agencies the aides may perform whatever nursing duties are approved by the organization for which they work, provided these duties are performed under the direct supervision of a nurse.

MISCELLANY

HUNTINGTON MEMORIAL HOSPITAL

Harvard University and the Massachusetts General Hospital have recently announced the conclusion of an agreement by which the main phases of the work in cancer treatment and research now being carried on by the Collis P. Huntington Memorial Hospital will be transferred to the Massachusetts General Hospital. The change will become effective as early in 1942 as possible.

"This step is being taken," the statement said, "in accordance with a long-held belief of both the University and the Massachusetts General Hospital that the care and treatment of medical specialties can be more efficiently handled as part of a large institution of general scope than in smaller individual units. Both the hospitals concerned have been major factors in the study and treatment of cancer in the New England area for many years; and it is confidently believed that the combination of their facilities will not only provide an improved service for patients suffering from malignant disease, but will also render such service more economically to the general community.

"Under the new arrangement, there will be transferred to the Massachusetts General Hospital the inpatient and outpatient services now available at the Huntington Memorial Hospital. By extension of its outpatient service, the Massachusetts General Hospital can readily accommodate all patients who have heretofore been using the Huntington Hospital; during the last year the latter cared for 14,000 outpatient visits. The Massachusetts General Hospital also has ample space in which to set up additional beds to equal the present complement at the Huntington Hospital; hence there will be no reduction in the number of beds available for the care of cancer patients in the community as a result of the change.

"The Laboratory and research work now carried on by the Harvard Cancer Commission through employment of certain funds of Harvard University will continue under supervision of that commission. Research activities under the direction of Dr. Joseph C. Aub will be carried on at the Massachusetts General Hospital in connection with the large and well-organized tumor clinic which that hospital has been operating for many years. The remainder of the varied research work of the Harvard Cancer Commission will be continued in conjunction with the Harvard Medical School.

"The equipment of the Massachusetts General Hospital, including its modern 1,000,000-volt x-ray machine, will be available to all patients, and the Harvard supply of radium, heretofore used at the Huntington Hospital, will be transferred to the Massachusetts General Hospital."

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1941

Diseases	October 1941	October 1940	Five-Year Average*
Anterior poliomyelitis	45	7	13
Chicken pox	571	491	367
Diphtheria	9	20	16
Dog bite	902	845	778
Dysentery, bacillary	43	21	43
German measles	35	26	28
Gonorrhea	351	374	455
Measles	373	619	298
Meningitis, meningococcal	10	5	5
Meningitis, other forms	2	—	—
Mumps	335	199	179
Paratyphoid infections	6	3	2
Pneumonia, lobar	192	219	229
Scarlet fever	467	266	291
Syphilis	450	394	430
Tuberculosis, pulmonary	342	223	243
Tuberculosis, other forms	33	30	30
Typhoid fever	11	6	6
Undulant fever	6	3	5
Whooping cough	555	645	491

*Based on figures for preceding five years.

Geographical Distribution of Certain Diseases

Actinomycosis was reported from Boston, 1; Reading, 1; total, 2.

Anterior poliomyelitis was reported from: Acushnet, 3; Adams, 1; Andover, 1; Boston, 4; Bourne, 1; Brockton, 2; Cambridge, 1; Carver, 1; Chelsea, 1; Danvers, 1; Dedham, 1; Falmouth, 1; Fall River, 1; Lowell, 1; Lynn, 4; Malden, 1; Merrimac, 1; New Bedford, 2; North Attleboro, 1; Norfolk, 1; Pittsfield, 3; Saugus, 1; Southboro, 1; Springfield, 1; Taunton, 2; Wakefield, 1; Walpole, 1; Ware, 2; Wellesley, 1; West Bridgewater, 1; total, 45.

Anthrax was reported from: Holyoke, 1; Springfield, 1; total, 2.

Diphtheria was reported from: Boston, 1; Bourne, 1; Fall River, 6; Worcester, 1; total, 9.

Dysentery, bacillary, was reported from: Adams, 1; Arlington, 1; Boston, 3; Dracut, 2; Ipswich, 5; Lawrence, 1; Lowell, 1; Melrose, 8; Springfield, 1; Worcester, 20; total, 43.

Infectious encephalitis was reported from: Lynn, 1; Springfield, 1; total, 2.

Meningitis, meningococcal, was reported from: Boston, 1; Brockton, 1; Ipswich, 1; Fort Devens, 1; New Bedford, 1; Quincy, 1; Randolph, 1; Waltham, 1; Woburn, 2; total, 10.

Meningitis, other forms, was reported from: Brockton, 1; Taunton, 1; total, 2.

Paratyphoid infections were reported from: Boston, 2; Everett, 1; Fort Devens, 1; Lynn, 1; Malden, 1; total, 6.

Septic sore throat was reported from: Boston, 2; Fall River, 1; Hingham, 1; Medford, 2; New Braintree, 1; Salisbury, 1; Waltham, 1; Weymouth, 1; Williamstown, 1; total, 11.

Tetanus was reported from: Boston, 1; total, 1.

Trachoma was reported from: Boston, 1; Dedham, 1; Lynn, 1; total, 3.

Trichinosis was reported from: Attleboro, 1; Boston, 1; total, 2.

Typhoid fever was reported from: Boston, 3; Brockton, 1; Cambridge, 1; Fall River, 1; Fitchburg, 1; Norwood, 1; Springfield, 1; Westwood, 1; Worcester, 1; total, 11.

Undulant fever was reported from: Great Barrington, 1; Mendon, 1; North Adams, 1; Worcester, 3; total, 6.

Anterior poliomyelitis continued at a level above the usual seasonal incidence of nonepidemic years.

Chicken pox, dog bite and mumps showed record-high incidences, this being the second consecutive month for dog bite and the fourth for mumps.

Scarlet fever had the highest prevalence for October since 1935.

German measles, measles, meningococcal meningitis, paratyphoid infections, pulmonary tuberculosis, typhoid fever, and whooping cough were reported above the five-year averages.

Diphtheria and lobar pneumonia were reported below the five-year averages.

The incidences of bacillary dysentery and undulant fever were not remarkable.

NOTE

The election of Dr. George R. Minot, professor of medicine at Harvard Medical School, as president of the Inter-State Postgraduate Medical Association of North America was recently announced.

225
41

CORRESPONDENCE

HEALTH OF THE WORKER AND HIS FAMILY

To the Editor: I noted with great interest and satisfaction the inclusion in the December 11 issue of the *Journal* of an article by Mr. Bloomfield entitled "The Private Physician's Opportunity in Industrial Medicine" and another by Dr. Pinto and Mr. Bowditch entitled "Industrial Medicine." Also, your board saw fit to devote an editorial to this subject.

We have been frequently reminded that the present war is different from any other in which we have ever engaged and that there are two fronts: that defended by the armed forces and that supported by civilians, the most important of whom are those engaged in defense industries. There is a degree of satisfaction in this latter point, since every person has a definite sense of playing his part in winning the war and defending the freedoms for which we are fighting. Today, the boy who is found physically unfit for service, but who is by no means an invalid, can hold his head high with the sense that he has a duty and a service to perform that is second only to the man at the front. This is also true of older people and of women, and it is going to require the full measure of effort of a determined people, physically fit and with a high war morale, to win out against our powerful and treacherous foes.

Industrial hygiene is not a new field. Those concerned with this work, however, have quite generally been interested only in those diseases or injuries that arise because of certain inherent conditions within a particular industry. We are reminded by Mr. Bloomfield's article that there is "enormous waste of life and efficiency resulting from nonindustrial illness among workers." It is estimated that of the 400,000,000 man-days a year lost because of disabilities, only 5 or 10 per cent can be classified as due to specific industrial hazards. The major problem has to do, obviously, with the various forms of illness, such as respiratory infections, gastrointestinal disease and the like, that occur in all people but show an excess, oftentimes, among industrial workers. It is a familiar fact that disease prevalence varies inversely with income when this is below a certain level. We know that women in industry suffer from an excess of absenteeism six times that of men. If we are really going to make a contribution to the war effort, the greatest opportunity lies in the field of reducing the common illnesses of man. I am not, in this, belittling the value of setting up the necessary safeguards against chemical poisonings, dust hazards, physical injury and other specific industrial diseases, but I am saying that we must change the general philosophy that has prevailed and look realistically at the relative values of our efforts in this field, and that employers, employees, industrial physicians, private physicians, industrial nurses and all the rest of us must adopt a new point of view. There are the same possibilities of reducing sickness among the industrial workers who congregate together daily as there are in prevailing diseases in the general community. The field is as broad as the whole public-health program.

To study ways and means of assisting and furthering a complete industrial-hygiene program, the Health Division of the Massachusetts Committee on Public Safety has created the Committee on Occupational Hygiene, which comprises representatives from the Massachusetts Medical Society, employers, employees, industrial nurses, insurance companies, the health-education group and the Massachusetts Division of Industrial Hygiene. It is hoped that they may bring forth a program that will be constructive and helpful to all concerned in reducing the wastage of manpower resulting from all forms of preventable diseases among the laboring classes.

CURTIS M. HILLIARD, *Director*
Health Division, Massachusetts Committee on Public Safety
18 Tremont Street
Boston

REPORTS OF MEETINGS

PLYMOUTH DISTRICT MEDICAL SOCIETY

A regular meeting of the Plymouth District Medical Society was held November 13 at the Plymouth County Hospital at 11:15 a.m. The meeting was called to order by the president, Dr. G. A. Moore. The minutes of the previous meeting were read by the secretary, Dr. R. C. McLeod. Mention was made of the death of Dr. H. H. Burns, of Plymouth, in May, 1941.

Dr. Bradford Peirce presented a program of films and slides of tuberculous patients treated at the South Hanson Hospital by modern methods, including lobectomy, pneumonectomy, thoracoplasty and pneumolysis. These were illustrated by several cases with recovery. Dr. Moore made comment on the vastly improved death rate in tuberculosis in the past thirty years, attributing at least part of the improvement to surgical intervention, and touched lightly on lobectomy and pneumonectomy, which are reserved for well-selected cases; he added that, as a rule, the operative results are excellent.

The main speaker was Dr. J. C. McCann, of Worcester, chairman of the Committee on Medical-Care Costs Insurance. He gave an outstanding and vigorous plea for co-operation by all members of the society, which was well received.

EDWARD S. PERRY, M.D., *Reporter*

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

Dr. James C. McCann, of Worcester, chairman of the special committee concerned with prepayment medical-care costs insurance, spoke at a meeting of the Middlesex South District Medical Society on December 10.

The members of the society passed a resolution, made

by Dr. Charles E. Mongan, that supported the work of Dr. McCann and his committee. It was requested that this fact be published in the *New England Journal of Medicine*.

ALEXANDER A. LEVI, *Secretary*

BOOK REVIEWS

The Care of the Aged (Geriatrics). By Malford W. Thewlis, M.D. Third edition, entirely rewritten. 8°, cloth, 579 pp., with 50 illustrations. St. Louis: The C. V. Mosby Company, 1941. $6.00.

The author's long interest in old people is shown by the fact that he has rewritten this book, which first appeared in 1919. It consists of thirty-eight chapters grouped in five sections, and it claims to be "still the only recent book dealing with the medical care of the aged."

The first section, "General Considerations," sketches the value of old-age hygiene, the prevention of premature senility, prolongation of life, work for the aged, hobbies, economic problems and medicolegal relations. Many interesting observations are found, but in general the reviewer believes that the discussion suffers both from incompleteness and from repetition. Exercise is disposed of in five lines. Recreation is given one paragraph, as follows: "Recreation is an important factor. The aged brain becomes fatigued easily; a sophisticated play or film which causes mental strain should be avoided. The senescent mind reacts well to something lively and humorous." Heredity is discussed in several places. Furthermore, it is not always clear whether the author is thinking of the normal person of sixty, seventy or ninety, of the institutionalized pauper or of the senile dement.

The second section, "Miscellaneous Medical Problems," includes chapters on nutrition, nursing and therapeutics. The chapters on anatomic and pathologic changes in old age suffer seriously on comparison with the scholarly reports in Cowdry's *Problems of Ageing*. The third and fourth sections deal with infectious and noninfectious diseases (the latter are defined as allergy, alcoholism and focal infections).

In the fifth section, "Pathologic Conditions in Old Age," there are subtitles for practically every condition dealt with in standard textbooks of medicine and surgery, with numerous references to medical literature. Statements concerning the changes imposed by age on disease and on its treatment are often given as impressions and as recollections of individual cases drawn from a rich experience. They show good clinical judgment for the most part. Careful reading and rereading, however, leaves one wishing that there were more evidence of critical study and correlation.

The book cannot be highly recommended, since it is not a satisfactory guide to the care of the aged. On the road to geriatrics, it is "a landmark, not a guide post."

Natural Resistance and Clinical Medicine. By David Perla, M.D. and Jessie Marmorston, M.D. 4°, cloth, with 1344 pp. and 44 tables. Boston: Little, Brown and Company, 1941. $10.00.

This is a curious book. Its authors for some time have evidently been interested in what resistance to disease may be, and here, as they say, they have attempted to put down in print an analysis of many of the factors that are believed to determine or modify natural or acquired susceptibility to infection.

The task of putting together such a book is enormous. The authors quote more than five thousand references to current literature in the forty-six chapters that make up the volume. Almost every conceivable phase of resistance to disease is discussed, from the prevention and treatment of surgical shock to the role of copper, iron or manganese to resistance, or from the effect of psychic factors to the effect of age and sex, of endocrine glands or of vitamins.

This is the kind of medical text that one would wish to find in a library — useful for reference or to encourage browsing. It can have very little general appeal to students or practicing doctors. It deserves praise, however, as being an honest effort toward gathering a large conglomeration of literature and crystallizing therefrom a number of stimulating ideas.

New England readers may be interested to know that this is the first large American medical publication to be printed by Little, Brown and Company of Boston. For a book so large, its physical characteristics are handsome. It weighs no more than it has to for its size; the type is admirable; the indexing is adequate; the illustrations and tables are clear. The appearance of the book, therefore, carries on the fine tradition of expert book making upheld for so many years by its publishers.

The Principles and Practice of Ophthalmic Surgery. By Edmund B. Spaeth, M.D. Second edition, thoroughly revised. 8°, cloth, with 1149 illustrations and 6 colored plates. Philadelphia: Lea and Febiger, 1941. $10.00.

Effective surgery is consummated only when a comprehensive diagnosis is combined with surgical skill and ingenuity. In the field of ophthalmology, the internist, the neurologist and the ophthalmologist find a common diagnostic meeting ground. The author of this book wisely recognizes the importance of diagnosis, and he incorporates diagnostic considerations as the prerequisite for the choice and application of surgical therapy. The text carries an authors' index, as well as a general index.

Lucid writing, a wealth of well-chosen illustrations and freely given credits to authorities in their respective fields make this book the collective voice of modern workers everywhere, and an indispenable guide for every current practitioner of eye surgery. The twenty-six chapters of the book deal with anesthesia, reconstructive plastic surgery of the eyelids and socket, surgery of the lacrimal apparatus, surgery of the ocular muscles, cataract and glaucoma surgery, reattachment of a separated retina, extraction of intraocular foreign bodies and treatment by radium and surgery of neoplasms of the eye and its adnexa.

A Textbook of Ophthalmology. By Sanford R. Gifford, M.D. Second edition, revised. 8°, cloth, 470 pp., with 255 illustrations and 14 colored plates. Philadelphia: W. B. Saunders Company, 1941. $4.00.

The second edition of Gifford's excellent work corrects the typographic errors of the first edition, and is replete with many informative illustrations in black and white and in color. The author has rewritten portions of the book to cover advances in knowledge that have taken place since the publication of the first edition, notably in chemotherapy as applied to ophthalmology, and in the ocular manifestations of general diseases.

The practitioner and the medical student will find here concise, interesting and dependable information to guide them in understanding how to deal with the ophthalmic problems that arise in practice.

225
1